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THE MOSAIC OF ANDROGYNY*

Maleness Within the Female and Femaleness Within the Male

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LIKE other bisexual forms, the human species is divided into males and females according to the presence of testes or ovaries, with their accompanying external genitalia. Reproduction is the primary purpose of these opposed organ assemblages. But, in addition to the specific function of race perpetuation, each man and woman must likewise serve the law of self-preservation. This vital individual task, among primitive peoples at least, calls for different kinds of qualities that are adapted to the special relation maintained by each sex toward environment.

So far as one knows, the actual phenomenon of reproduction is achieved through the genital organs alone. A person's other task of survival depends on adequate adjustment with a complex environment, which includes human relations. The impulse to survive is expressed extragenitally by the man in manly fashion, and by the woman in womanly ways. The opposite and special endowments for these purposes are in general well known, and are displayed by differences between man and woman in morphology, physiology, immunity and psychology — or as somatic cellular sex in the total organism. This composite structure of masculine and feminine characters has been called "the mosaic of androgyny" (ἀρδνόσ = male; γυνη = female). The term is used because the nongenital qualities appropriate to each sex are never complete in a given man or woman to the exclusion of some evidence of the counterpart. Thus, traits that are ordinarily judged to be the man's may appear in the woman to form kaleidoscopic patterns with her own; the reverse is likewise true. The contrasting qualities have to do not only with outward design, structure and function, but even more significantly with the extragenital dynamics of the whole person. So far as the relation of human constitution to disease is concerned, the androgynous phase of sex seems to be of greater significance than the genital. And it is for this reason that the terms "andric" and "gynic" (adjectives formed from the joint word's component parts) have been chosen to designate the divergent organismal aspects of man and woman.

Within certain limits, the expressions of cellular sex in adults are modifiable by castration or its milder physiologic analogue, — the climacteric, — or by tumors of various endocrine glands. A good example of this is the greatly increased emphasis on andric characters in patients with adrenal tumors, as described by Gallais.[1] But even in his Case 3, the late effects of the tumor could not have been related to the existing broad shoulders and narrow hips. These andric characters must have been laid down in the genetic plan, or effected at an early embryonal stage by some intrauterine accident. It goes without saying that sex hormones exert a powerful influence on the entire organism. But the effects of castration, for example, are more extensive in the male. Furthermore, the castrated male tends to take on characters that in many respects are similar to the female. This "toward-female" capacity, however, is more marked in some castrates than in others. Among insects it is known that the various somatic insignia of maleness or femaleness may have no relation to the nature of the gonad. From all these observations it seems that sex is something more than the mere presence of a gonad. As Lillie[2] believes, sex is not "an irreversible predestination, but a quantitative over-

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balance in the direction of one sex or the other."

Andric and gynic characters strongly and subtly woven into the fabric of each one's personality are not unappreciated by laymen. Posture, gesture, voice and the flavoring of individual identities have long been observed and used as a means of classifying people in masculine or feminine categories. Moreover, from groups and audiences composed either of men or of women, the unerring impact of this bisexual otherness can easily be felt. But the awareness of it is more sharply focused in the impression made by a single person. One is quick to recognize the presence in a member of one sex of qualities properly allocated to the other.

To illustrate the divergence of andric and gynic impacts that radiate from groups, an excellent opportunity is afforded by a visit to a large medical clinic. Anyone who has worked long in hospitals has, no doubt, noticed the subtly different atmosphere that one senses in the men's and women's wards. There is an air of tranquillity in the latter. Neatness, decorum and patience fill the place. In some strange manner, women seem more at home there, more appropriate to bed in daytime than men. As one enters the quiet ward, one notices that all the patients seem to be reclining easily in their beds — they are mostly supine, with arms and hands crossed on the midriff or stretched resignedly beside the body. All are relaxed among their pillows. When they turn their eyes and heads to view one's approach, the expressions are not overcurious, and the motions of those who do move are unhurried and deliberate. Then, as one scans the group of patients, one's attention is sharply arrested by the woman in the third bed to the left. She is a vigorous-looking person of about fifty. A shock of white hair, cut short behind and at the sides, surmounts the powerfully modeled forehead and heavy dark eyebrows. Almost imperiously, the restless eyes observe what is going on, and the vigorous mouth and lower jaw are energetically engaged alternately in chewing gum, making thorny remarks and offering innumerable suggestions. The entire personality exudes a force that cuts sharply across the ward's passive atmosphere. The andric qualities of this person, expressed in the masculine modeling of the head, the vigorous gestures and the projection of total organismal energy, are easy to observe.

And when one enters the male ward, greater activity is at once apparent. Things are not so neat and particular as in the women's ward. Some patients are lying with knees up, others are on their sides supporting themselves by one elbow, still others, with hands clasped behind their heads and elbows wide, are uncomfortably propped by their pillows. Occasionally, one man calls across to a friend in another bed, a radio is switched on, a patient turns awkwardly to see what an intern is doing to his neighbor. Costly of outgoing energy are all these attitudes, which accomplish little. Possibly, they express the need for satisfaction in motion, a response to the man's biologic urge to project his life force on the universe in an effort to arrive at some self-appointed goal.

Sitting at the ward's center table are three patients. Two are playing pinochle and slapping the cards down with gusto. The third attracts attention by the contrast of his attitude and appearance. This patient is an average-sized man, with large hands out of proportion to the limited thickness of his frame, and with a large pale face marked by small features. He sits quietly, hands clapsed in his lap and watches the game with a tolerant and gentle smile. Often, he wags his head in mild rebuke, as though to say, "Now, children, not too roughly." When one asks him his occupation, he replies in a high-pitched husky voice with neat diction, "I'm a blacksmith, Sir." A more careful inspection reveals a paradox between this man's trade and total personality. Instead of knotty muscle, his arms and back display a smooth panniculus. Rounded shoulders, slightly prominent belly and mons veneris above curving hips and thighs bespeak a strongly feminine morphology. He patiently waits for his discharge, watches but never joins the ward activities, and creates no trouble for anyone.

From the foregoing description of differences between the impact of the andric or gynic thing that emerges from massed men or massed women, it is possible to recognize that energy, common to both groups, is utilized in quite different ways. It is not the varying magnitude of energy capacity that is the significant difference between the two phases of the androgyny. In many cases, women may be actually stronger than men. But the feminine pattern of energy utilization is fundamentally different from that of the man. The former tends to conserve and build up energy stores and to spend it cautiously. The latter, on the other hand, is prodigal of his virile forces.

The concept of the andric and gynic differences in energy utilization is not new to biologists. Thus Doncaster[8] reflects it in the statement that the egg is large, quiescent and stores up energy. Sperm, on the other hand is small, actively motile and spends energy. It will be noted that these basic differences in the two opposing initial cells are

characteristic of the average adult male and female in practically all species. In the matter of conduct, for example, everyone is familiar — especially the woman — with man's strenuous pursuit of his objective. Once his interest becomes fixed on his heart's or mind's desire, nothing else matters but its achievement. He moves vigorously toward it, overcoming obstacles at any cost, leaving a trail of wreckage behind. The woman, on the other hand, as man well knows, tends to be static. She is not easily mobilized, and therefore often keeps him waiting. Woman must preserve a safer and more stable situation for the security of the offspring and herself. She not only conserves her own strength but reaches out her hand to stay the man's impetuosity, to retain his energy for the supply and defense of her protectorate. Geddes and Thompson[4] have expressed the same thought by saying that femaleness is correlated with preponderant anabolism, maleness with emphatic catabolism.

This view is supported by Riddle's[5] observations on differential basal metabolic rates between males and females. He found that rates for males were consistently higher than those for the opposite sex. If, then, one accepts the notion that in the extragenital phase of human beings the androgynous differences between man and woman are to be found in their types of body form, their conduct and their mental attitudes, one can proceed to a more detailed consideration of individuals of each sex.

Andric and Gynic Qualities

Morphology

Viewed from in front or from behind, the basic silhouettes of the male and female forms can be respectively described as one of angular rectilinearity or of curving ovoid. The lateral aspect of the woman presents perhaps less of the ovoid outline, but a greater emphasis on localized curving convexities. From in front, the man's arms appear to be hanging freely dependent from the shoulder points, and at the elbow there is little or no obtuse angle known as the carrying angle. His pelvic breadth is notably narrower than that of the square shoulders, and the lower extremities are straight or slightly bowed at the knee. When the heels are approximated the space between the lower extremities presents a characteristic outline (Fig. 1). The inner belly of the gastrocnemius is more prominent than the outer, and the outer curve of the calf bends sharply in toward the external malleolus. In the woman, on the other hand, the shoulders are more sloping, and the upper extremity instead of hanging from the acromion point seems to extend the downward moving neck-shoulder modeling in a continuous curving line. The carrying angle is well marked, so that the forearm and hand clear the prominent outward curve of the hip and thigh, which in turn springs from well above the iliac crest. The far wider hip line is determined in part by the bony structure and in part by the greater distribution of fat over the lower abdominal, pelvic and upper thigh areas. The lower extremities are rounded, and when the heels are together, the thighs are approximated from the crotch to the knees, which are pressed in close apposition. Between the knee and ankle a space appears, owing partly to the genu valgum and partly to the less emphatic inner belly of the gastrocnemius. The outer line of the leg sweeps in an even, continuous curve from knee to outer malleolus.

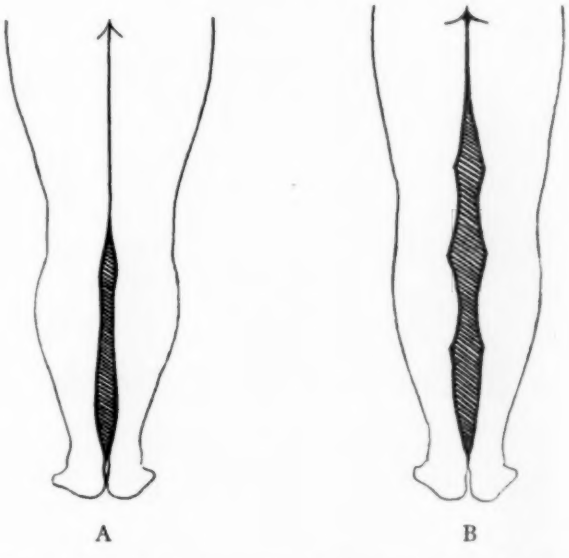

Figure 1. *Showing Interspace of the Approximated Lower Extremities in Women* (A) *and in Men* (B).

Besides these more general contours or silhouette contrasts (Figs. 2 and 3), differences of surface modeling between man and woman are well known. In men such observable localized bosses or protuberances as may appear are chiefly due to the well-developed muscles, which are covered only by a thin layer of subcutaneous fat. What have been ordinarily designated as secondary sex characters, namely, breasts, mons veneris, girdle and thigh fat deposits, on the other hand, constitute the otherness of a woman's surface modeling. The woman's muscles are not large and knotty, and may be completely hidden beneath a fairly thick, smooth panniculus. The distribution and quantity of facial and body hair constitute another well-known set of morphologic criteria that differ between men and women.

Physiologic Panel

Some physiologic phenomena show andric and gynic differences. Perhaps the most notable of these is the basal metabolic rate, which, as mentioned above, is known to be higher for males than for females. It is also usually accepted that red-cell counts and hemoglobin levels are lower for women than for men. Of this, Riddle[5] states: ". . . present knowledge establishes the probability that these excess values [that is, red-cell and hemoglobin] in males cling to maleness because they are a real part of the metabolism machine and because sex difference takes its basis and origin in metabolic difference." Here the oxygen-carrying capacity seems to indicate a connection with the metabolic level, and the pulse rate has usually been said to be higher for women than for men. The notion that metabolic rate and sex difference are closely related has been noted by numerous observers. Furthermore, the rate in both males and females can be lowered by prolonged inactivity of the animals, as shown by Lusk and DuBois,[6] but such effects of rest are more striking in the male. As Riddle[5] says, "Any sex changes which may occur as a direct result of prolonged inactivity should be in a male-to-female direction." Child[7] believes that differences in susceptibility to external toxic agents are characteristic features of different levels of physiologic gradients, or more specifically that a relation exists between susceptibility and basic metabolic rate:

> With certain qualifications and limitations, it appears to be true that the rate of oxidation is in some degree a measure of the rate of living. It has also been shown that in the less highly specialized protoplasms susceptibility to certain ranges of concentration or intensity of external agents is an indicator of rate of oxidation and may be used as a rough comparative measure of differences in rate. There is, therefore, a real experimental basis for the statement that susceptibility is in general a measure of rate of metabolism or more particularly oxidation.

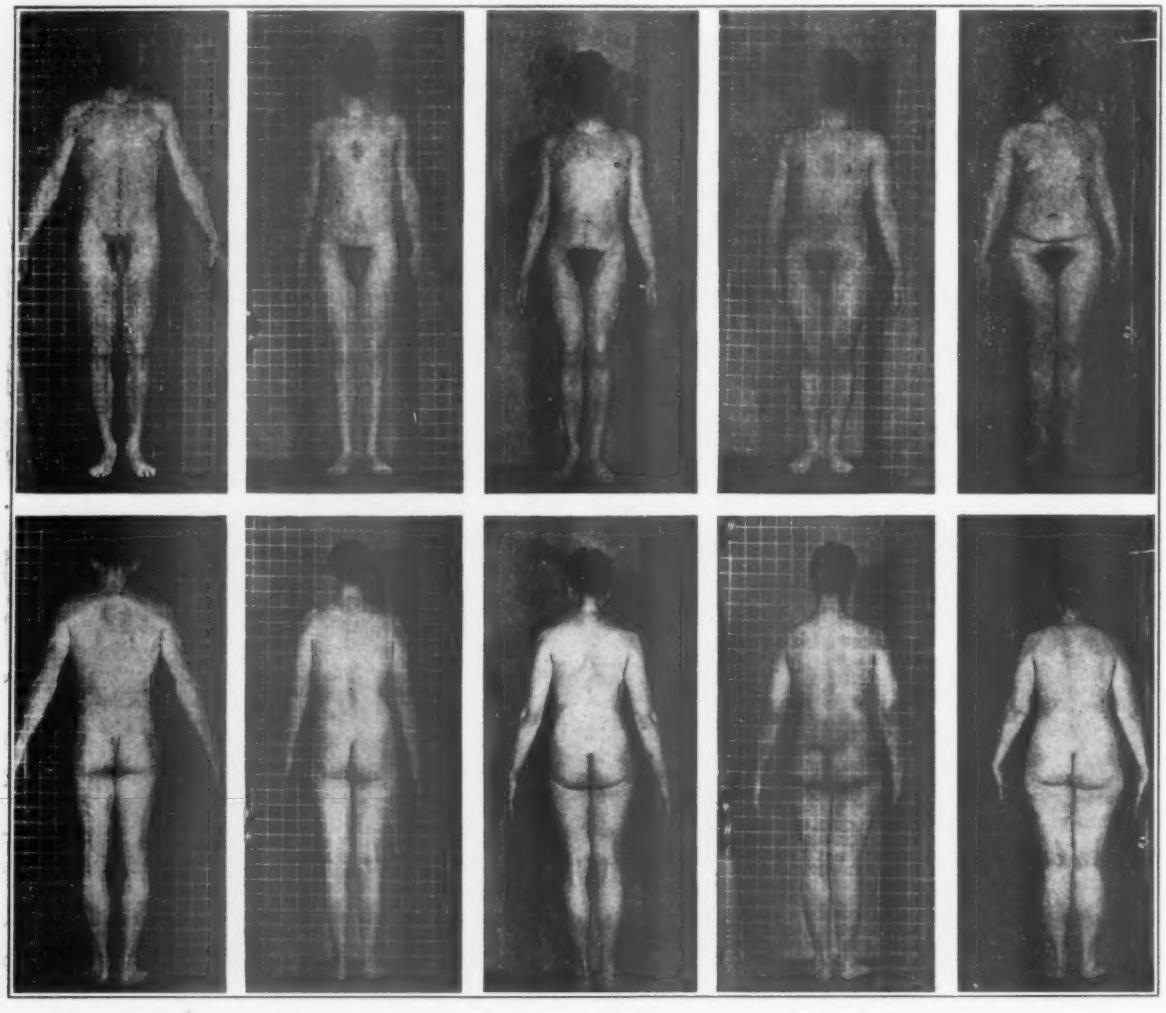

FIGURE 2. *Showing Increasing Emphasis on the Gynic Factor in the Male Morphology.*

Thus, all the observations and experiments related to metabolism and sex difference support the notions of the biologists, Doncaster[3] and Geddes and Thompson,[4] that gynic values relate to quiescence and conservation of energy, andric to its expenditure.

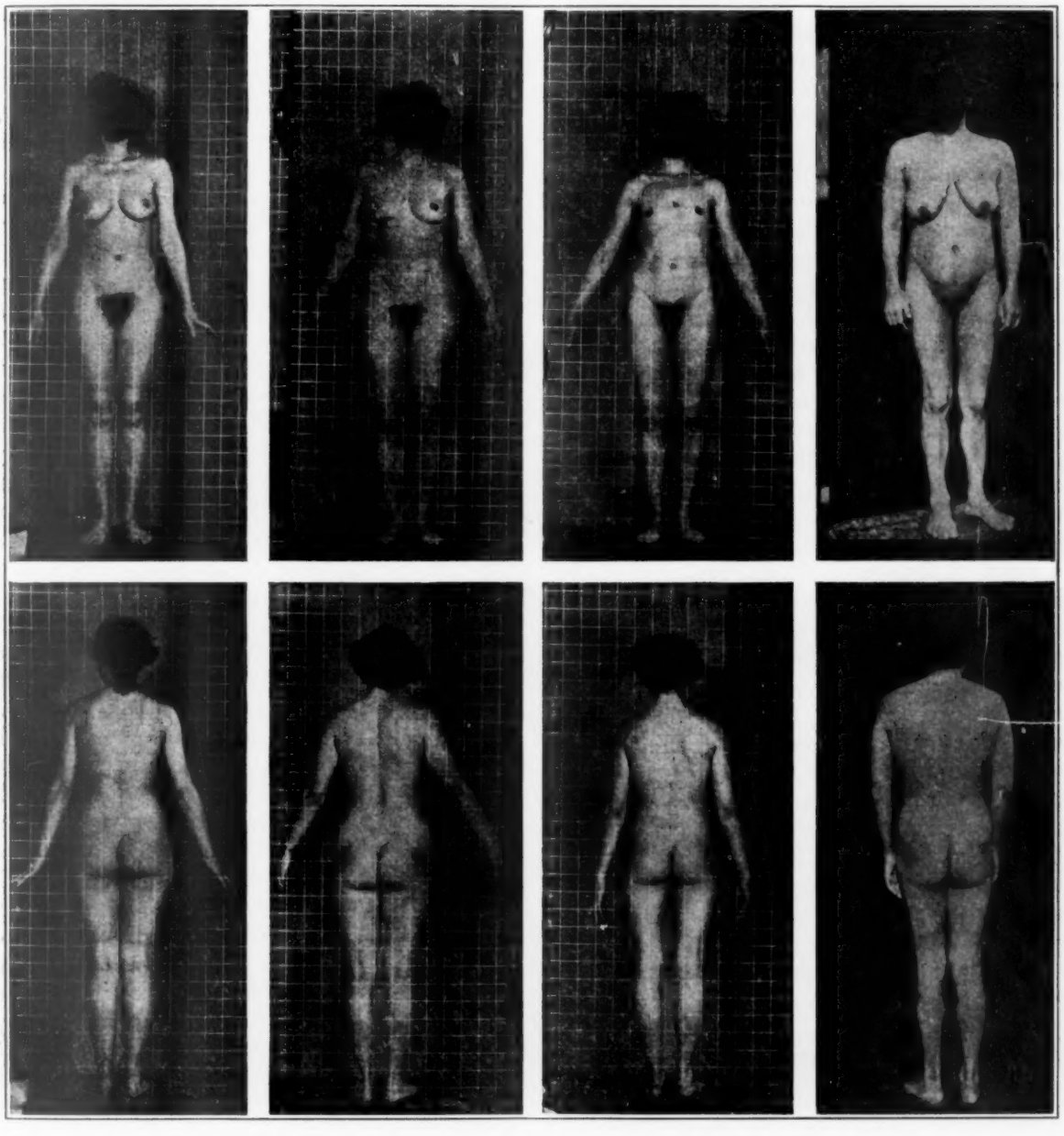

FIGURE 3. *Showing Increasing Emphasis on the Andric Factor in the Female Morphology. (Figure at Right Illustrates a Case of Gallais Double Adrenal Tumor.)*

Psychology

In the psychologic panel, the task of differentiating andric and gynic characters is not altogether an easy one. Terman and Miles[5] undertook to assay the opposing qualities by means of various questionnaires and word-association tests. Their findings are interesting and show for example the following generalizations.

> Masculinity in men at either of two educational levels is associated with positive interest in active and mechanical pursuits; it is also associated with indifference to artistic and cultural pursuits. Femininity in men is the reverse of masculinity in its relationship to interests. Masculinity in women . . . is associated with positive rather than negative interests, with activity and, in the more highly educated, especially with intellectuality. Femininity in women shows the reverse of masculine trends. It appears associated with less intense positive interests and these are directed towards the arts of home and social life. Mental fem-

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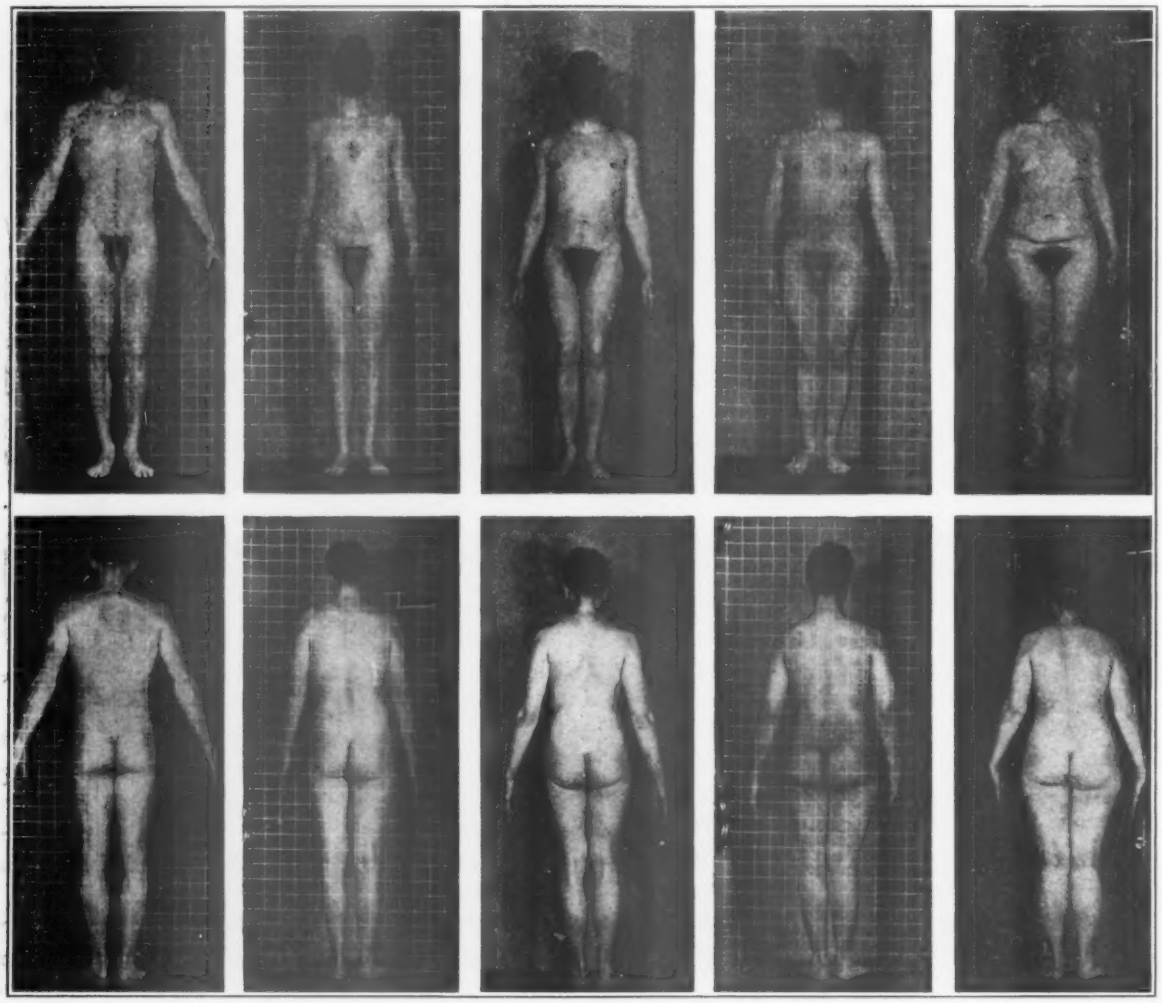

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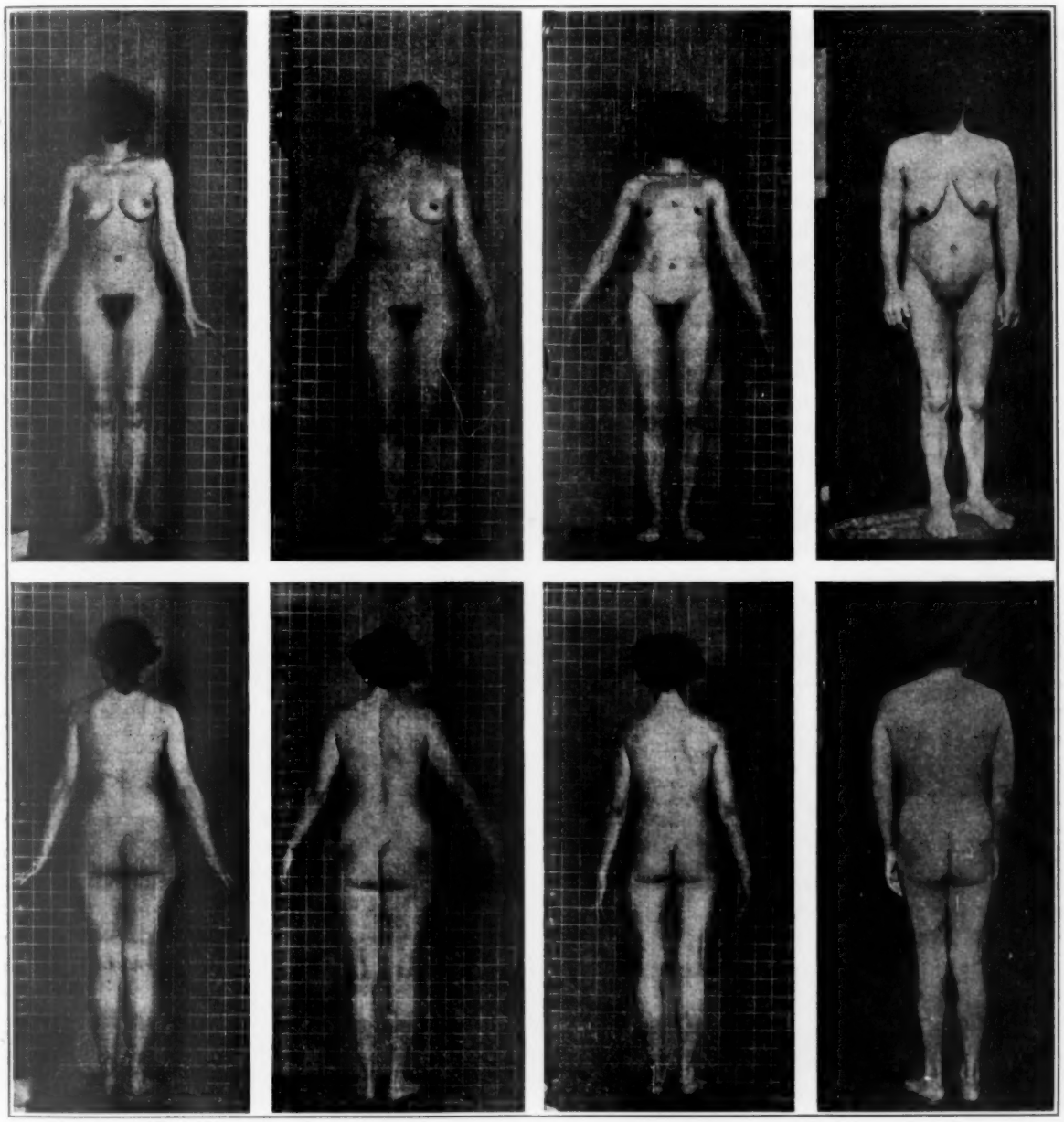

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ininity is expressed also in indifference to active scientific and in the better educated, intellectual interests.

There is, too, in the popular conception of maleness the quality of direction or leadership to which is applicable Murray's[9] term "regnancy." Or it might be called dominance, as opposed to the more commonly presumed feminine qualities of subservience and docility. Intelligence and reason, however, cannot justifiably be classed as essentially male; neither can intuition and emotion be allocated exclusively to women, for all these mental functions are extragenital possessions of every person. Some of these variable qualities no doubt are products of specific hormones. On the other hand, recognizable criteria of a different sort, perhaps conditioned, also seem to enter the picture. Thus, man's traditional notion of woman's nature and hers of his, and what in consequence each may expect of the other in the social and economic structure and in personal relations, inevitably stamp each with a reciprocally accepted cognition of sex. This picture, projected by a woman of what to her is a man, or by a man of what to him is a woman, varies widely in terms of racial, national and cultural background. Indeed, it seems to take on the order of an ethnic trait. Nevertheless, it is possible that from an infinite variety of blendings of andric and gynic psychic values there may result preponderant projectivity or conservatism, determination or irresolution, directness or evasiveness, brutality or gentleness that will produce well-defined patterns of psychic personality. These may then be correlated with andric and gynic qualities in the other panels of the total organism. The observable signs of these complete patterns are to be sought, not only in morphology and physiology, but also in the person's attitude toward life and in his manner of merging himself in his constantly changing environment.

Clinical Applications

It was earlier suggested that if, instead of the genital mark, the androgynous mosaic were used as the criterion for division of individuals into sex groups, many of our present sex classifications in medicine might need revision. In this respect, the challenge offered to clinicians by the allocation of diseases according to sex is of greatest interest. There have been numerous studies of this matter; one of the most thorough being that of Mobius.[10] Moreover, in the textbooks of medicine, the paragraph on incidence usually states that the disease in question is commoner in one sex than in the other. After an exhaustive inquiry in which he admits complete inability to explain the occurrence in men of diseases strikingly more frequent in women, Mobius concludes that if it were not for alcohol and syphilis, men would be less often sick and would live longer than women! Notwithstanding this naïve capitulation to a selected stress of environment, however, it should be noted that in his discussion of muscular dystrophies he remarks that muscle is notably "manly tissue; its failure difficult to explain."

That Nature apparently has more use for females than for males has long been known. From start to finish the latter show greater susceptibility to disease and a higher death rate. Thus, for example, studies of the sex ratio indicate that there are 160 early male abortions and 130 male stillbirths for every 100 female ones. Furthermore, at term, there are 104 or 106 living boys for every 100 girls who survive, but at the end of the first year, only 100 boys remain alive for every 103 girls. Bakwin[11] reports that among infants under one year of age 130 to 134 boys die for every 100 girls. This is a sweeping toll, which exists at a time when the genital phase of sex amounts to an almost negligible part of the total sex endowment. One gains the impression that the organismal or androgynous phase of sex must contain some curious relation between andric and lethal forces. One can accept, I think, as a limited factor against a man's chance of survival, Mobius's[10] belief that males are, in general, more exposed than girls and women to hazards, alcohol and syphilis. Also, it is known that developmental anomalies are commoner in males than in females, as though it were more difficult to build a male than a female. Thus, for example, in a series of 2000 cases of pseudohermaphroditism ten to one possessed the male gonad (Mobius). Furthermore, there is likewise that small group of rarer maladies that display the interesting phenomenon of sex linkage. The following conditions reported by Davenport[12] and others are dominant in males and recessive in females: coloboma, color blindness, night blindness, congenital nystagmus, ichthyosis, hemophilia, webbed toes and Gower's muscular atrophy. There remains, however, for further consideration a great group of more or less common diseases that appear year after year in the wards of general hospitals everywhere. Among these, one finds a varying incidence in men and women, changing from an equal distribution to more or less extremes of emphasis in one sex or the other.

Figure 4 charts a group of diseases that have been selected simply on the basis of their differ-

ential frequency in the two sexes. But it should be remembered that the figures are based on the concept of sex in terms only of gonad type. In other words, these are men because the gonad is testicular; those are women because they bear ovaries. The concept of the nongenital androgyny as a constitutional factor has not been introduced. Yet the very nature of the shifting curve apparent in the chart, which moves almost continuously from one sex preponderance to the other, suggests a susceptibility gradient rather than two diametrically opposed sex types. Furthermore, in many cases

FIGURE 4. *Differential Sex Incidence in Disease Susceptibility.*

it has been possible to show that persons of one sex who develop a disease commoner in the opposite display notable emphasis on the inappropriate androgynous component of their own.

The scope of this paper does not permit a detailed discussion of each disease shown in the chart so that only two or three will be offered.

The patient with gallstones is one example. It is generally considered that women are more prone to the disease than men, in the proportion of about 5 or 6:1. Moreover there is an old medical saying that the commonest type of woman to be affected is "fair, fat and forty." When, however, a man who is the subject of cholelithiasis appears, one is often struck by the strong emphasis on gynic characters in his total person. In addition to evidences in skeletal measurements there may be other gynic marks of contour, fat distribution, gesture, facial expression and turn of mind. Such men may be adequate sires, thus supporting their claim to masculinity in the genital phase. But in the rest of the organism strong gynic emphasis appears. One might infer from these considerations that as a general principle the more completely a person is differentiated toward maleness or femaleness, the less should be his or her predisposition for those diseases in which the opposite sex factor is a contributing one. Almost the reciprocal of the foregoing situation appears among the subjects of peptic ulcer, an illness in which the sex ratio is high, the ratio of men to women being 5 or 6:1. Here again the afflicted women usually possess evidence of andric emphasis. It is interesting, too, to note that there is a tendency in ulcer families to produce a preponderance of male offsprings, whereas more female descendants appear in families of gallstone patients.[13]

In alcoholism the sex ratio is also high. Most statistics give the ratio of men to women as 6 or 8:1. But many observers will recall that the impression made by drunken women is a more masculine than feminine one. In my own experience with inebriates, almost every woman presented unmistakable emphasis on andric characters. Interesting, too, is the fact that whereas for the whole alcoholic series men significantly preponderate, in Korsakoff's psychosis the ratio drops to 2:1. But I have not directly observed such cases in women for the purpose of evaluating the androgynous mosaic. This curious reversal of andric-gynic emphasis in a special aspect of the human being's reaction to alcohol finds a parallel in rheumatoid arthritis and the spondylitis of Marie–Strümpell. Thus, in the general incidence of rheumatoid arthritis, 3 women are affected to 1 man. But in the cases of spondylitis, the ratio of men to women is 10:1. Heberden's nodes are found almost exclusively in women and, as originally pointed out by the great English clinician, usually at the climacteric. Such a phenomenon no doubt may be considered to be more directly determined by the hormone change (modification or curtailment) than by the original balance of somatic cellular androgyny. The age factor likewise must enter the picture, but much is still to be learned concerning the biologic relation of age and sex.

Gout, on the other hand, is almost entirely confined to the masculine sex. Concerning the androgynous balance of patients with this malady, I have met some difference of opinion. Two of my colleagues tell me that of the few female

gouty patients whom they have seen all presented strong emphasis on gynic features, with minimal emphasis on the andric. On the other hand, Jamieson[14] refers to Motley's picture of Margaret of Parma, "with her imperious temper, her masculine appearance, her moustache and her gout." It is possible that in my colleagues' cases the andric emphasis was much less marked in the morphologic than in the other panels.

When one attempts to explain the possible significance of disease incidence in relation to androgyny, the notion arises that the nature of the disease may express the different manner of energy manipulation that was earlier associated with each sex. Thus, men are commonly more vulnerable to diseases involving the apparatus for spending energy in action, whereas those that are related to energy storage and resting tissue metabolism arise chiefly in women. From the point of view, then, that sex appears to be a fundamental quality of somatic tissue, apart from its genital purpose, it is possible to contemplate the susceptibility to certain diseases as a further example of such bisexual somatic endowment.

Perhaps this dual possession may also be a mixed blessing. Concerning external agents, no doubt, andric or gynic properties do determine many patterns of reaction to life that are necessary or appropriate for the good of the individual man or woman. In primitive societies, however, the necessity for division of labor between man and woman for the care of offspring called out the opposite characters of each in widely separate spheres of action. All the outgoing energy production of the man was required to provide food, to build his cabin and to fight in defense of his home and family. The woman's energy on the other hand overflowed serenely through the house, surrounding her young with benevolent protection. Her instincts kept the larder jealously stored. Her swift intuition was alert to sense approaching danger; threatening problems were met out of stored experience by a remarkably successful empiricism. At that stage of history, men had comparatively little use for gynic qualities, or women for andric, so far as problems of adjustment to environment were involved. But these more or less unused opposite characters have become valuable to each sex with the increasing mechanization of contemporary civilization. Struggles of man against Nature have given place to those of man against man, and have confronted the individual with new kinds of adaptation demands. More and more, all occupations are being invaded by both sexes. In some of these, women are forced to swing their latent andric factors into action; in others men must employ their gynic values. Police officers, business executives and lawyers, for example, are callings that attract women whose androgynous mosaic is highly colored with andric emphasis. The culinary art, horticulture, nursing and, finally, the practice of medicine are occupations toward which men lean when their gynic values are well developed. Of these, medicine is one of the most interesting. For many years it has been followed almost exclusively by men. Yet it is quite obvious that much of the success of the physician depends on his gynic values of intuition, understanding and impulse to conserve. It may be because of woman's increasing perception of her latent andric forces in the intellectual field that she now is entering the medical profession in steadily mounting numbers.

The purpose of the foregoing remarks has been to point out that this balancing pair of opposites — an Heraclitean enantiodromia — presents no cause for shame or embarrassment, but rather contains important values for every individual of each sex. Consequently it would be well if each person could recognize his or her androgynous pattern and permit its andric or gynic components to function appropriately in respect to the momentary life situation.

There is, however, a further sphere in which these two powerful forces may interact, not with environment, but on one another within the isolation of the self. Here in the innermost citadel, where the ego strives to preserve its essence, threats to the inviolability of the personal identity are challenged and parried. The intensity of this protective response is often reflected in the most extreme and grotesque compensatory efforts. These result apparently because for the average man there is no threat to self-preservation more potent than the implication of inadequate or declining virility. The notion that feminine qualities are inherent in his personality is one not easily accepted by most men. An excellent example of the early appearance of this sort of emotional distress is that which appears in boys who tend to plumpness and whose external genitalia develop slowly. And it has been my experience that such children never wholly lose the sense of inferiority established in those early days, notwithstanding subsequent achievement of physical and functional genital adequacy. Individual effort, however, to compensate for a deep psychobiologic awareness of essential inadequacy is a matter that is exceedingly difficult to evaluate mathematically. It remains inevitably individual,

an infinite variable. At present, it cannot be brought into the same statistical category with the morphologic and physiologic observations herein reported. But the principle may be illustrated by the effort of a certain soldier in World War I to satisfy himself that he was secure in the biologic sense. He was a congenital eunuchoid whose gracile form displayed the delicate nonmuscular contours of a young girl. He was accepted for service, and soon found himself an infantryman at the Chateau Thierry front. Not content with holding his place in the line, he requested the special duty of messenger between the advanced observation posts and the trenches. This peculiarly dangerous and fatiguing task he performed with distinction. On his return to peacetime occupation in America, the first job he selected was that of a ship-loading longshoreman.

Of somewhat similar nature is the interesting observation that a majority of our peptic-ulcer patients are drawn from the ranks of taxi-cab drivers, policemen and firemen. These occupations demand constant output of energy in aggressive and often dangerous effort. Consequently, it is understandable that all these occupations expose their representatives to inner doubts concerning the validity of their essential beings. The intensity of these doubts may well relate to the actual balance of the andric and gynic forces that is present within the individual, and to his constitutional sensitiveness to the threat of his gynic component. From this conflict arises a fear in the subconsciousness of the potential peptic-ulcer patient, for example, that when the crucial test comes he will fail to play the masculine role adequately for the preservation of either his body or his soul (ego ?), or both. Now it has been my observation that among these patients the emphasis on the gynic component, especially within the psychologic panel, has been unusually high — a paradox to the nature of the employment.

* * *

Thus, it appears that, in respect to external agents, andric and gynic forces possess highly specialized and harmonizing reaction potentials. But within the person the two factors may come to grips with one another in destructive conflict. The intrinsic male fear is of his gynic component, which, if he could but accept and understand it, might prove instead to be a powerful ally. In view of these considerations, it becomes easier perhaps for each man and woman to appreciate how important to successful negotiation of life relations is an awareness, if not a complete understanding, of the phenomenon of androgyny. No doubt the andric and gynic factors, like other individual endowments, serve a biologic purpose. But depending on a person's repudiation or acceptance of them, they may become the source of destructive conflict or reservoirs from which energy may be wisely released toward creative work and equanimity.

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PNEUMONIA IN MASSACHUSETTS: 1900–1940

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THE advances recently encountered in the treatment of pneumonia have been so spectacular that we have not dared to take our eyes from the road ahead, lest we fail to negotiate another sudden turn. Yet behind us lie facts that must not be forgotten, because they concern themselves with the very road over which we have been traveling, and there is no more useful way to visualize our progress than to retrace the actual path by which we have come. Modern pneumonia discussions have concerned themselves principally with selected groups or selected problems within the larger mass of the people as a whole. This is as it should be, for only by such selection can facts be established in detail. The experience of an entire population as expressed by its mortality figures, on the other hand, may be utilized to demonstrate the mass reaction of millions of people to the respiratory hazards of their environment. Although such experiences must be cautiously interpreted for pneumonia in Massachusetts, it is proper and may be profitable to speculate concerning the degree in which current habits and efforts have influenced the great changes that have taken place. It is especially pertinent to examine these relations while they are still fresh in mind.

To present a simplified concept of our pneumonia experience, the mortality curve for "all forms" of the disease has been chosen for illustration. Although this choice is open to criticism on several grounds, I believe that there is no better index of what has actually been occurring in Massachusetts. Morbidity rates are notoriously unreliable and incomplete. The separation of the lobar pneumonia cases is still accomplished by criteria on which the clinician and the pathologist do not always agree, and probably has more to do with the speed of invasion and the intensity of reaction within the host than with the circumstances of definition. Whether one prefers a clinical, anatomic or even a bacteriologic definition of lobar pneumonia, one will find that its curves pattern themselves very closely after that established for all forms. It is also of interest that the same pattern has been followed by the curves for measles, whooping cough and other respiratory infections, each of which may appropriately be considered an integral part of the curve for all forms, and to have come under the same influences that have operated on the others. The accompanying chart (Fig. 1) is therefore considered the best available illustration of the behavior of pneumonia — including lobar pneumonia

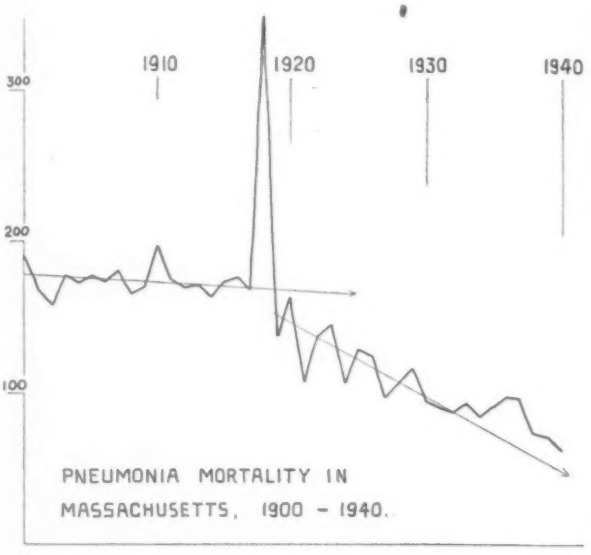

FIGURE 1.

— in Massachusetts for the present century. In addition, the curves for the registration area of the United States closely parallel this curve.

During the first seventeen years of the century, the pneumonia death rates were relatively constant. The total variation in Massachusetts was less than 15 per cent, and the trend was but very slightly downward. Then the epidemic of 1918 showed on what an unstable basis the relation between the pulmonary system and the outside world rested. The more one looks at this chart the more one appreciates the difficulty of estimating the influence of cause and effect in this disease. Involved explanations are needed to show why other clinics could not duplicate the therapeutic results achieved with unconcentrated serum at the Hospital of the Rockefeller Institute[1] in 1917; why two successive years in a single clinic led to opposite conclusions on the value of serum therapy, as they did on the pneumonia service at the Boston City Hospital[2] in 1920 and 1921; and why the general practitioners of medicine

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exhibited seeming indifference to what the enthusiasts of twenty years ago considered the great therapeutic contribution of the day. State-sponsored serum treatment was begun in 1919 in Massachusetts. In the light of what has happened, it is well that serum therapy was not universally adopted at that time, for it would now be difficult to escape a correlation between such an adoption and the very evident change in the mortality trend that took place (Fig. 1).

In the decade between 1920 and 1930, a remarkable series of reductions in pneumonia mortality occurred, reaching a point that was 50 per cent lower than the average of the first two decades. The trend of the curve for these ten years turned so sharply downward that it would, if projected, cross the base line in 1950! Of course the prospect of any such projection is fantastic, but it is important to remember that the major part of the reduction of the last forty years took place in this one decade. Whether the influenza epidemic had removed people with pulmonic susceptibilities, as has been suggested, or whether the general nutrition and resistance of the population were enhanced by changed habits and living standards is mere speculation. Better treatment may have been a factor, but not specific treatment, because very little serum was used in Massachusetts during this period; nor was any other therapeutic method employed on a large scale. One recalls enthusiastic claims for physical, chemical and biologic agents, but none of them enjoyed sufficiently widespread use to be reflected in this experience of the population as a whole. Most clinicians will agree that the therapy of the 1920 to 1930 decade was highly empiric, but that under it pneumonia somehow became a kindlier disease. Comment began to be heard on the mildness of the pneumonia seasons. The florid pneumonias, with full lobar distributions that lasted for a week or more, still occurred, but less frequently, whereas the abortive one-day or two-day pneumonias appeared, or at least were recognized more generally.

After 1930, it was plain that the pneumonia rates in Massachusetts could not continue along the trend that had been established for them following the influenza epidemic of 1918. There were too many people in the older age groups for whom pneumonia was a friend. As Osler[3] said: "Taken off by it in an acute, short, not often painful illness, the old escape those cold gradations of decay that make the last stage of all so distressing." The Massachusetts rates were also already lower than those of most other parts of the country, but as one recalled the explosion of 1918 one had a sense of insecurity. It was like an Indian summer: one was sure that it could not last. It probably would not have lasted if the present effective methods of treatment had not developed in rapid succession.

During the first five years of the Massachusetts Pneumonia Study,[4] from 1931 through 1935, the volume of serum treatment was not high; 798 cases were treated, and the total of pneumonia deaths in the State was 19,309 — a ratio of approximately 1:24. During the next two years, 1936 and 1937, serum was given in 957 cases, and the total deaths amounted to 8394 — a ratio of 1:8. This was the first period in which anything approaching an effective volume of serum therapy was applied in Massachusetts, and yet this treatment was accompanied by mortality rates that, in 1936 and 1937, were higher than they had been since 1930. This is true both with the figures for lobar pneumonia and with those for all forms. It may mean that the Indian summer was coming to an end in 1936. Those who collaborated in the Pneumonia Study believe that the rates would have been higher still, had not a comprehensive program of serum administration been under way. It therefore seems to be a fair conclusion that in 1936 and 1937 the pneumonia program minimized what might otherwise have been a greater natural variation toward seasons of increased pneumonic severity.

This is a point of more than academic interest, and it should be made at this time before one forgets just what really did happen between the two wars. The major part of the mortality reduction was spontaneous and rapid, and had nothing to do with antipneumonia efforts. It was due to natural causes, if living standards and habits may be included in this category. After 1934, a reaction in the severity of the disease occurred. It would probably have been a greater reaction, had it not been curbed by the gathering power of the pneumonia program. In 1938, with rabbit and other serums for the higher types of pneumococci, in 1939 with sulfapyridine, and in 1940 with sulfapyridine and sulfathiazole, the curve was again brought to new low points.

The rate for 1940, 61.6 per hundred thousand population, is the lowest yet recorded in Massachusetts. The amount of serum dispensed by the State was 40 per cent less in 1940 than in 1939. There is no such accurate measure of the amount of sulfonamide drugs used in 1940, but common knowledge would place its volume well above that of 1939. In other words, the best results were coincident with an increased usage of drug and

a decreased volume of serum treatment. This means that the community as a whole benefited by the large-scale application of a relatively safe and inexpensive and easily administered drug, the exhibition of which did not need to wait for bacteriologic study. The simplicity here implied may be open to scientific criticism, but it remains a practical fact, and suggests that a more effective antipneumonic treatment for the population as a whole had been awaiting the discovery of a method that would be simple enough for general application. The application of an involved science is as ineffectual as that of an involved art.

It has been said, "There was a steady drop, year by year, in the deaths . . . since the pneumonia programs began."[5] As an unqualified statement, this is debatable. The mortality record so far does show a steady drop since the use of sulfonamide therapy began. The record also shows that the spontaneous amelioration of pneumonia is the outstanding phenomenon of the century to date. This same natural amelioration is plainly written into the mortality returns for all the air-borne infections, including that chronic one — tuberculosis. Our respiratory security, if we have any, must rest largely on this natural foundation. It is the basis of a better health level for the people as a whole. Its versatility embraces all the air-borne diseases, and its total benefits are manifold. Even after excluding smallpox and diphtheria, which have been artificially prevented, the natural amelioration of the air-borne infections is already contributing a greater share to the prolongation of life than that provided by the almost complete elimination of the enteric fevers. For some reason, this epidemiologic similarity in the behavior of the air-borne diseases has never been commented on. Much has been said of the lessened severity of scarlet fever, but is its present behavior relatively more benign than that of measles, whooping cough or even pneumonia? Fears are sometimes expressed that the virulence of scarlet fever may return, and we are frequently warned of the next influenza epidemic, being lugubriously reminded that we do not know how to prevent the disease that scourged us in 1918. This is true, but in January, 1941, we had a visitation the virulence of which was, for a few people, fully as deadly as anything that was experienced in 1918. Clinically, malignant influenza was in our midst, just as the so-called "malignant scarlet fever" occasionally still appears, but some natural communal force resisted its spread.

Thus, there is much evidence to confirm a belief that during the present century pneumonia has been increasingly confronted by a collective resistance in the host. Early in the last decade, this resistance stabilized the pneumonia death rates in Massachusetts at a level 50 per cent lower than that of the first decade of the century. The pneumonia program and especially the widespread application of chemotherapy have now contributed to a still further depression of the death rates from pneumonia.

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THE FREQUENCY OF POLIOMYELITIS IN PREGNANCY*

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BOSTON

INDICATIONS of the widespread and more or less uniform dissemination of the virus of poliomyelitis are seen in such epidemiologic features as the geographic prevalence and age distribution of the disease; in the gradation from frank to mild or suspected abortive forms of the clinical disease; and in the far more extensive occurrence of subclinical infection, as indicated by the development of serologic immunity in those who do not have the disease in any of its recognized forms.

The limited and selective occurrence of the frank disease indicates that some added circumstance determines clinical or subclinical infection on exposure to the virus. Certain of these selectivities point to differences in the person exposed rather than differences in exposure. A tendency to familial occurrence indicates that susceptibility may be inherent; seasonal and climatic variations in the frequency with which exposure to the virus results in the paralytic disease points to a physiologic function rather than to a fixed anatomic character; the association of the disease with persons of a certain constitutional type is suggestive of endocrinologic differences; the occurrence of poliomyelitis following surgical procedures on the upper respiratory mucosa indicates that temporary mucous-membrane conditions may affect susceptibility[1]; and, finally, because of the implication of the upper respiratory mucosa as the portal of entry of the virus, the suspected selectivity seen in the association of poliomyelitis with pregnancy, in view of known mucous-membrane alterations due to estrogenic changes of pregnancy, suggests that autarceologic susceptibility to poliomyelitis may reside, at least in part, in the economy of estrogenic substance.

As is well known, pregnancy affects the development or progress of a number of diseases, either favorably or unfavorably. These effects may be secondary to mechanical influences of the gravid uterus, they may be due to nutritional stresses, or they may result from intrinsic physiologic changes, more specifically some of the marked endocrine changes of pregnancy. Thus, the improvement seen in certain cases of pulmonary tuberculosis has been ascribed to mechanical effect, such as splinting of the thorax; whereas the severity and fatality of pneumonia are perhaps less

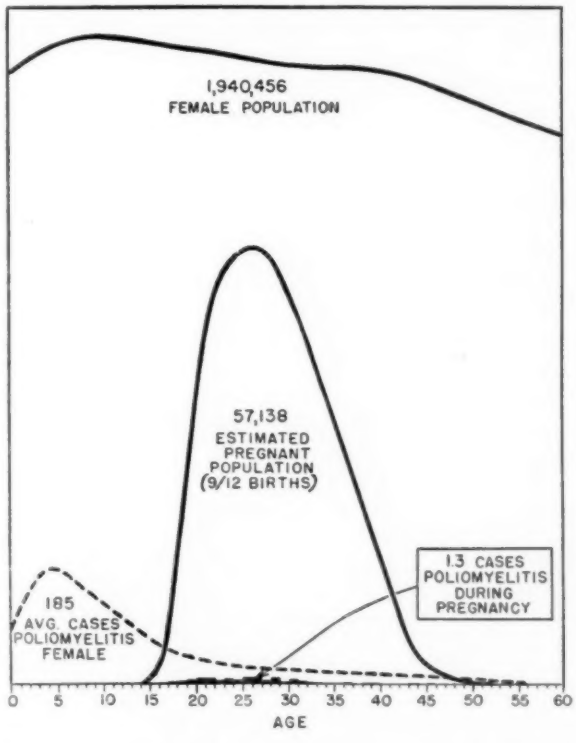

FIGURE 1. *Expected Poliomyelitis during Pregnancy in Massachusetts.*

clearly attributed to immobilization of the diaphragm by the gravid uterus. The added nutritional demands may induce polyneuritis in patients already on a minimal diet, or this deficiency disease may be secondary to hyperemesis. Physiologic changes, including increased blood dilution and volume and increased cardiac output, with decreased hemoglobin, serum protein, nonprotein nitrogen and red cells, account for the effects on heart disease. Certain endocrine disorders are initiated by, or are a continuation of, endocrine changes of pregnancy: toxic goiter may be activated, and pituitarism may be influenced. In still other diseases, no satisfactory explanation

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is forthcoming for the effects noted. The mechanism of the so-called "therapeutic effect" of pregnancy on syphilis, as well as the resistance exhibited by pregnant animals to experimental infection with syphilis, is unknown. Because of the frequency of association, pregnancy has been regarded by some as an important predisponent to lethargic encephalitis.[2, 3]

The numerical infrequency of paralytic poliomyelitis, especially in view of the fact that the disease is preponderantly one of younger age groups, makes its chance occurrence in pregnancy small. The average annual occurrence of poliomyelitis in Massachusetts for the ten-year period 1928–1937 was 455 cases, of which an average of 185 cases were in females. The number of births and stillbirths in the same population per year is approximately 76,000. Three-fourths of this number represent an approximation of the number of women pregnant at a given time. On a basis of the age distribution of poliomyelitis and the age of pregnancies, the estimated coincidence of the two conditions, as shown in Figure 1, at any given age is fractional, the total for all ages being 1.3 cases per year. But since this estimate is based on the incidence of poliomyelitis, of which only half the cases were paralytic, it may be seen that the expectancy of paralytic poliomyelitis in pregnancy is less than 1 out of 1000 cases of poliomyelitis, and less than 1 out of 50,000 pregnancies.

In reviewing the literature, 28 cases of poliomyelitis associated with pregnancy have been encountered, and an additional 28 cases have come to notice either by observation or personal communication (Tables 1 and 2). Since these cases have been collected incidentally, no estimate of the frequency of poliomyelitis in pregnancy can be drawn from them. A good many represent individual case reports, and some have been mentioned in connection with other studies of the disease. The incompleteness of the record of poliomyelitis in pregnancy is further suggested by the fact that in the literature certain cases diagnosed as the well-known polyneuritis of pregnancy,[20] because of residual paralysis or fatal outcome with respiratory paralysis, possibly were actually cases of poliomyelitis.

TABLE 1. *Cases of Poliomyelitis in Pregnancy from the Literature.*

CASE NO.	AUTHORITY	PLACE	AGE OF PATIENT	TIME OF ONSET	OUTCOME
			yr.	*mo.*	
1	Wickman[4]	—	27	6th	Death (6th mo.)
2	Schell[5]	Philadelphia	26	7th	Normal delivery
3	Hartman[6]	—	—	7th	—
4		—	—	7th	—
5		—	—	8th	—
6		—	—	8th	—
7		—	—	9th	—
8		—	—	4th	Death (4th mo.)
9	Mueller[7]	Nauru	—	9th	Normal delivery (term)
10		Nauru	—	9th	Normal delivery (term)
11	Renault and Martingay[8]	—	23	5th	Normal delivery (term)
12	Zimmermann[9]	Germany	22	9th	Normal delivery (term)
13	Miller[10]	—	—	3rd	Normal delivery (term)
14		—	—	5th	Cesarean section (6th mo.); death of child.
15	Ehrenfest[11]	Missouri	18	6th	Normal delivery (term)
16	Hornung and Creutzfeldt[12]	Germany	20	8th	Cesarean section
17	McGoogan[13]	Nebraska	24	3rd	Normal delivery (term)
18		Nebraska	32	3rd	Normal delivery (term)
19		Nebraska	24	3rd	Premature delivery, death of child
20	Brahdy and Lenarsky[14]	New York	22	9th	Forceps delivery
21		New York	23	4th	Normal delivery (premature)
22		New York	19	2nd	Abortion (therapeutic)
23		—	—	Post partum (5 days)	Symptoms in child (9th day)
24	Guttmann[15]	Silesia	23	8th	Death
25	Pette[16]	—	—	3rd	Death
26	Klein and Sittig[17]	Germany	25	9th	Normal delivery
27	Morrow and Luria[18]	New Jersey	28	5th	Forceps delivery (term)
28	Ruhl[19]	Germany	27	8th	Normal delivery (term)

The only outbreak in which the frequency of poliomyelitis in pregnancy has been studied was in Detroit in 1939.[21] A total of 528 cases were recorded, of which 255 were paralytic. Four cases occurred during pregnancy. In Table 3 are shown the female population, the estimated number of pregnancies, the expected coincidence of poliomyelitis with pregnancy, and the observed cases in the various age groups. Although this occur-

rence is over four times the expectancy, the number involved is too small to be considered conclusive. But the finding is in line with other evidence presented, suggesting that pregnancy may be one of the predisposing influences to paralytic poliomyelitis.

This suspected selective occurrence is in accord with other selectivities suggesting that susceptibility to paralytic poliomyelitis may reside in a disturbance of some physiologic function, which may be subject to fluctuations in the patient, is endocrine in nature, and is operative through effects on mucous membrane. The known mucous-membrane changes in pregnancy, which are attributed to estrogenic changes, and the experimental production of alterations in the genital and nasal mucosas of monkeys by the estrogens, — because of the implication of the nasal mucosa as the portal of entry of the virus of poliomyelitis, — have formed the basis of two sets of experiments in an attempt to determine the nature of the factor responsible for susceptibility to paralytic poliomyelitis: tests of the effect of artificially induced changes on the susceptibility of monkeys to intranasal instillation of virus; and comparative urinary estrogen assays on poliomyelitic patients and normal persons.

The injection of estrogenic substance into castrate immature female monkeys was found to enhance resistance to intranasal instillation of virus.[22, 23] It is not known whether, on the one hand, the particular preparation used, the dosage and the manner of administration were sufficient to give changes that could be considered optimal so far as enhancement of resistance is concerned; or whether, on the other hand, such changes are entirely artificial and quite beyond what could be expected to exist naturally. However, since the experimental observations agree with epidemiologic implications, it is believed that the artificially induced conditions may perhaps be considered as reflecting conditions of resistance in the natural disease. A small number of comparative urinary estrogen assays have been done on poliomyelitis patients and normal subjects. The results indicate a higher excretion of estrogenic substance in the group of poliomyelitic cases.[22]

The question may well be raised why, if the administration of estrogen protects castrate monkeys, the higher excretion of estrogen found in poliomyelitic cases and characteristic of pregnancy should not confer a similar benefit. No convincing answer can be given. It may be noted, however, that the hormonal status of the pregnant woman differs from that of the nonpregnant, as well as the castrate animal, in a variety of ways. For example, pregnancy is dominated more by the corpus luteum hormone than by estrogen.

TABLE 2. *Cases of Poliomyelitis in Pregnancy from Personal Records.*

CASE NO.	PLACE	AGE OF PATIENT	TIME OF ONSET	OUTCOME
		yr.	*mo.*	
1	Vermont	32	7th	—
2	Vermont	25	7th	Child born lame
3	New York	26	Post partum (5 days)	Low forceps delivery (chloroform)
4	Michigan	—	6th	Cesarean section (7th mo.); death of child.
5	Massachusetts	—	9th	Poliomyelitis in child (12 days)
6	Massachusetts	—	Post partum (1 day)	Cesarean section
7	Massachusetts	30	4th	Premature delivery; paralysis and death of child.
8	Massachusetts	19	5th	—
9	Ohio	"Young"	2nd	Abortion (7th mo.); dead fetus.
10	—	20	4th	—
11	Florida	16	4th to 5th	Premature delivery (6th mo.); death of child.
12	New Hampshire	23	9th	—
13	France	—	—	—
14	—	20	6th	—
15	Vermont	—	6th	Cesarean section (8th mo.); death of mother and child.
16	Massachusetts	35	6th	Normal delivery (term)
17	Massachusetts	24	5th	—
18	Maine	—	—	Cesarean section
19	Iowa	33	5th	Forceps delivery
20	New Jersey	27	5th	Forceps delivery
21	Vermont	26	8th	Normal delivery (term)
22	Illinois	22	9th	Respiratory paralysis; forceps delivery and death of mother.
23	Colorado	26	7th	Normal delivery (term)
24	Massachusetts	23	7th	Respiratory paralysis; death of mother and child.
25	Michigan	24	3rd	Normal delivery (term)
26	Michigan	16	6th	Normal delivery (term)
27	Michigan	26	1st	Cesarean section (5th mo.); death of child.
28	Michigan	26	7th	Cesarean section

Pituitary growth-hormone secretion, as well as prolactin, is enhanced during pregnancy. It may be stated, in short, that the end effect of several interacting variables, one of which may be increased estrogen, might actually be different from increased estrogen alone. In this particular case, the administration of estrogen to castrate animals approaches the latter condition, whereas conditions in the natural disease involve the interaction of a number of hormones, of which increased urinary output of estrogen may be only one manifestation.

TABLE 3. *Paralytic Poliomyelitis in Women, Detroit, 1939.*

AGE	FEMALE POPULATION*	ESTIMATED NO. OF PREGNANT WOMEN	NO. OF FEMALE PARALYTIC CASES	EXPECTED CASES IN PREGNANCY	OBSERVED CASES IN PREGNANCY
yr.					
0–5	71,971	0	34	0.0	0
5–10	73,2[illegible]	0	36	0.0	0
10–15	66,871	11	26	0.004	0
15–20	63,866	1[illegible]89	8	0.174	1
20–25	76,394	5,426	7	0.497	1
25–35	153,462	10,852	4	0.283	2
35–45	118,797	3,950	0	0.0	0
45–55	64,840	75	0	0.0	0
Totals	689,472	21,703	115	0.958	4

*Based on figures for 1930 census.

SUMMARY

Seasonal, climatic, familial and constitutional selectivities in the distribution of paralytic poliomyelitis among those exposed to the virus point to differences in the persons exposed rather than to differences in exposure. Bulbar poliomyelitis following tonsillectomy and adenoidectomy, in view of the implication of the upper respiratory mucosa as the portal of entry of the virus, suggests this mucosa as the seat of operation of susceptibility.

Fifty-six cases of poliomyelitis associated with pregnancy are cited, 28 from the literature and 28 from personal records. The time of pregnancy when the disease occurred is unknown in 2 cases. Only 9 cases were recorded in the first trimester of pregnancy, whereas 19 cases were in the second trimester and 23 in the third. Three cases occurred post partum. Thus, the latter months of pregnancy appear to be chiefly concerned, although it must be borne in mind that the data for the first months may be discrepant.

The manner of collection precludes statistical analysis, but it is estimated that the chance coincidence of the two conditions is roughly 1 in 1000 poliomyelitic cases and 1 in 50,000 pregnancies. In a study of the frequency of poliomyelitis in pregnancy in the Detroit outbreak in 1939, the estimated expectancy of coincidence was less than 1 case, and 4 cases were observed. The suspected association with pregnancy, in view of accompanying mucous-membrane alterations due to estrogenic changes, suggests that autarceologic susceptibility to poliomyelitis may reside in the economy of estrogenic substance. Experimental effects of estrogenic substance on susceptibility to intranasal instillation of virus are in accord with this concept.

Because of the difficulty in establishing the significance of numerical frequencies in studies of this sort, the present report is intended to raise the question of the frequency of poliomyelitis in pregnancy, in the hope that similar studies will be made in other outbreaks.

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CLINICAL NOTE

AN ELASTIC CHEST GIRDLE FOR RIB FRACTURES*

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THE treatment of fractured ribs by adhesive strapping is so generally accepted, and on the whole is so satisfactory, that I have hesitated to report a retentive chest girdle used in treating such injuries. However, since for several years the girdle has proved to be a more comfortable form of treatment than the conventional strapping, as well as a more efficient means of immobilizing the chest, it seems to have special value. The girdle also has the advantage of being adaptable to cases in which the use of adhesive strapping is definitely contraindicated.

The idea of using a girdle to immobilize rib fractures is not new, although this form of treatment has received little recognition, and the use of the girdle has tended to be limited to those cases in which adhesive strapping is objectionable. Immobilizing belts and girdles of various designs and materials have been recommended by Knowles,[1] Funston,[2] Hammond,[3] Waugh,[4] Welti[5] and Christensen.[6]

In our clinic, the girdle is used in the treatment of all fractured ribs. When more than a single rib is broken, the position is maintained by increasing the width of the binder. The use of the girdle solves the problem of treatment when burns or abrasions are associated with the fracture, when the patient has a hairy chest or a tender skin, or when the respiration is embarrassed.

Patients find the binder extremely comfortable, and they promptly return to work. No pain is experienced on movement of the thorax, and there is no feeling of constriction, such as that when adhesive strapping is used. The man who does heavy work may tighten the binder during the day and loosen it at night. Immobilization is assured, because there is no tendency for the girdle to slip, as there is with adhesive strapping.

A more detailed description of the elastic girdle than that given in Figure 1 is hardly necessary. In width, it varies from 10 to 20 cm., depending on the number of ribs fractured. The girdle is easily and quickly made from readily obtainable material, and it costs very little. It is easily fitted, since the elasticity and the long range of buckling space allow for adjustment to a chest of any size. In its application, it should be tightened until there is no pain on forced inspiration or expiration. Because of the ease of adjustment, the girdles may be made in advance and kept on hand. When sufficient healing has taken place to ensure immobilization at the site of the fracture, the girdle is gradually loosened, and finally removed.

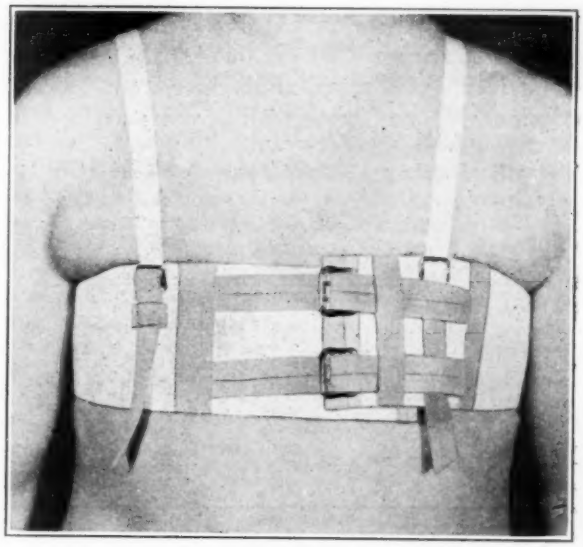

FIGURE 1. *Elastic Girdle Applied to Chest.*

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MEDICAL PROGRESS

DIABETES MELLITUS

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STATISTICS

THE death rate for diabetes in the United States reached 25.6 per 100,000 in 1939, with a total of 33,395 cases, thus exceeding 23.8, the previous highest figure, which was attained in 1938. One death in 41.5 was assigned to diabetes. In 1938, diabetes ranked ninth as a cause of death, but by 1939 it displaced premature births and became eighth. The positions held by diabetes in 1900, 1938 and 1939 are shown in Table 1. It requires little imagination to see that diabetes will soon displace tuberculosis and pneumonia, and then it will be exceeded only by arteriosclerosis in the heart, brain and kidneys, and by cancer and violence. Yet this very growth in incidence may detract from its recognition, because so few diabetic patients die of their disease that other diseases — which are complications or coincidental, like cancer and tuberculosis — may claim recognition before it and displace diabetes as the primary cause of death. Private clinics may therefore be the chief source in the future of reliable statistics on the disease. For statistics on diabetes, the seventh edition of Joslin, Root, White and Marble's[1] book on the treatment of diabetes mellitus presents recent data in considerable detail.

TABLE 1. *Deaths per 100,000 Population from the Chief Causes of Death in the Registration Area of the United States in 1939, as Compared with the Figures for the Same Causes in 1938 and 1900.**

DISEASE	1939		1938		1900	
	RANK	RATE	RANK	RATE	RANK	RATE
Heart disease	I	276.1	I	268.9	IV	132.1
Cancer	II	117.8	II	114.6	VIII	63.0
Cerebral hemorrhage	III	88.0	IV	85.7	VII	71.5
Nephritis	IV	83.1	V	77.2	V	89.0
Violence (accidents, suicides and homicides)	V	70.9	III	94.1	VI	96.0
Pneumonia	VI	59.4	VI	67.5	II	180.5
Tuberculosis (all forms)	VII	47.2	VII	48.9	I	201.9
Diabetes	VIII	25.6	IX	23.8	XXVII	9.7

*Prepared with the co-operation of the Statistical Bureau, Metropolitan Life Insurance Company.

The number of new cases for the year 1940 is estimated at between 50,000 and 60,000 by Mr. Herbert H. Marks, of the Statistical Department of the Metropolitan Life Insurance Company.

The remarkable alteration in the age distribution at death of diabetic patients in the United States for the last twenty years is shown in Table 2. There were approximately only one fifth as many deaths in the first decade of life in 1939 as in 1919, one fourth in the second and third, one third in the fourth, three fifths in the fifth, and six sevenths in the sixth; not until the seventh decade are deaths now more numerous. Conversely, there were 33 per cent more deaths in 1939 in the tenth decade, nearly 80 per cent in the ninth decade and 60 per cent in the eighth decade.

TABLE 2. *Percentage of Deaths from Diabetes, Classified according to Decade of Age at Death, in the Registration Area of the United States in 1919 and 1939.**

AGE	1939			1919		
	TOTAL	MALES	FEMALES	TOTAL	MALES	FEMALES
	%	%	%	%	%	%
Under 10	0.6	0.9	0.5	2.9	3.4	2.5
10–20	1.6	2.0	1.3	5.2	6.2	4.3
20–30	1.5	2.0	1.2	5.4	6.2	4.6
30–40	2.2	2.6	1.9	6.1	7.1	5.2
40–50	6.4	6.7	6.3	10.0	10.2	9.8
50–60	18.7	17.3	19.5	21.0	19.8	22.0
60–70	33.0	30.9	34.3	27.4	25.8	28.8
70–80	28.3	29.0	27.8	17.7	16.8	18.4
80–90	7.3	8.2	6.7	4.1	4.1	4.1
90–100	0.4	0.5	0.4	0.3	0.3	0.2
Number of deaths	33,395	12,558	20,837	12,683	5,769	6,914
Death rate per 100,000	25.5	19.1	32.0	14.9	13.3	16.5

*Prepared with the co-operation of the Statistical Bureau, Metropolitan Life Insurance Company.

The median age at death of patients with diabetes in New York City is advancing. Between 1904 and 1921, inclusive, and between 1922 and 1939, inclusive, there was a significant change equivalent in range to three to five years for men and two to four years for women, owing largely to the introduction of insulin (Table 3).

TABLE 3. *Median Age at Death of Diabetic Patients in New York City.*

PERIODS	MEDIAN AGE AT DEATH			
	MALES		FEMALES	
	Lowest	Highest	Lowest	Highest
1904–1921	56.1	59.1	58.2	61.0
1922–1940	59.2	64.7	60.4	65.4

All articles in this series will be published in book form; the current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. $4.00).

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For 927 deaths occurring, in the experience of Joslin, Root, White and Marble, between January 1, 1937, and March 29, 1940 (the Hagedorn Era), the average age at death was 64.8 years, and the duration of the disease 12.5 years, in contrast with 46.7 years and 6.1 years, respectively, for the period June 1, 1914, to August 6, 1922 (the Allen Era).

The total number of persons with diabetes in New York City is estimated to be somewhere between 50,000 and 75,000, or 6.8 to 10.2 per 1000 population.

In a systematic study based on reports of the physicians of the Berlin Medical Society, Umber and his associates[2] report that in the population of Berlin (4,346,074) there were 14,153, or 3.2 per 1000, diabetic persons — in 1916 in Charlottenburg, the estimate was 2.3 per 1000. Insulin was used in the treatment of 37 per cent. The necessity of supplying insulin to diabetic patients to increase their working capacity has been stressed by Umber's group. In the diabetic clinic of the West End Hospital in Berlin, only 3 per cent of patients were unable to work on account of their disease. The number of Jews in Berlin was estimated at 82,788, and among them 3.5 per 1000 were diabetic; insulin was used by 43 per cent.

Education

The present is the Era of Education in diabetes. Two large monographs on diabetes have recently appeared, along with an increasing number of schoolbooks, textbooks and manuals for patients. Camps for children are far more numerous, exceeding eighteen in number, and probably are more largely attended. The number of articles on diabetes, whether clinical or experimental, is so voluminous that a reviewer is swamped and sometimes almost breathes a sigh of relief to see a periodical that has nothing related to diabetes on its pages.

Boards of health are increasing their diabetic activities, and in New York City last winter more than two hundred popular talks on the disease were sponsored by the Board of Health, in co-operation with medical societies. For some years, Cincinnati has been particularly active in this regard. In New York City many years ago, Dr. Charles F. Bolduan was largely instrumental, working from his position in the Board of Health, in bringing about, with the help of the New York Academy of Medicine, the organization of the New York Diabetes Association.

More instruction in diabetes is given in hospitals. More nurses are engaged in teaching diabetic patients, and more classes have been organized for their benefit. In addition to this work for patients, more time is set aside for the study of diabetes in nurses' training schools and in medical schools.

Insurance companies have a vital interest in diabetes. This year, one of them has undertaken an educational program that is nationwide in scope and on a broader and yet more detailed basis than has ever before been attempted. It is evident that the interest not of one but of many insurance companies is being awakened. Their accurate statistical methods are sorely needed in diabetes. It would be even more valuable if they made a searching inquiry into the deaths reported as diabetic and the deaths of persons who earlier were known to have had diabetes.

For several years in England, there has been an organization for diabetic patients known as the Diabetic Association. It issues the *Diabetic Journal*,* sold for a shilling, which contains practical articles on diabetes suitable for patients and the public. The association and the *Journal* continue to function despite the war.

During the last few months, the American Diabetes Association has been incorporated; its first meeting was held in Cleveland last June preceding the meeting of the American Medical Association. This society is national in scope and is best described by Articles II and III of its constitution:

> ARTICLE II. *Purpose.* The objects of this association are: (1) to disseminate among physicians information relative to the diagnosis and treatment of diabetes by means of meetings, bulletins and the publication of papers in scientific journals, and through a central office, which would at all times make available information concerning various aspects of diabetes; (2) to educate the laity in the early recognition of diabetes and in the realization of the importance of medical supervision; (3) to secure and co-ordinate the active co-operation of associated groups acceptable to the Trustees in the educational and organizational phases of the association; (4) to make and publish statistical surveys of diabetes; (5) to encourage and support clinical, experimental, sociological and statistical studies by means of grants; (6) to encourage the adequate treatment of diabetes and the establishment of summer camps for children.
>
> ARTICLE III. *Membership.* The membership of the association shall consist of four classes: (1) active members; (2) associate members; (3) honorary members; (4) corporate members. Only active members in good standing shall have the right to vote. Any physician with proper qualifications may be elected an active member of the association by a majority vote of the Trustees. Active members shall pay stipulated annual dues. All those interested in the aims and purposes of the association, whether physicians, scientists, statisticians, dietitians, nurses, social workers or laymen, may become associate members upon election

*The *Journal* is published quarterly at 124 Baker Street, London, W.1.

by the Trustees, and upon payment of stipulated annual dues. Honorary membership may be conferred by the Trustees on those individuals who have rendered distinguished services in medical or other fields related to diabetes. Associated medical or welfare organizations, civic or educational groups and insurance companies may be elected to corporate membership of the association in recognition of the auxiliary services which they may render to the association.

The Prevention and Cure of Experimental Anterior-Pituitary Diabetes

In last year's review,[3] reference was made to the unpublished work of Haist, Campbell and Best,[4] of Toronto, and of Lukens and Dohan,[5] of Philadelphia, on the prevention and cure of the experimental pituitary type of diabetes of the dog and cat. To recapitulate briefly, Best and his co-workers found that when insulin was injected into a dog at the same time as anterior-pituitary extract, diabetes failed to appear, and no destructive changes occurred in the islands of Langerhans; Lukens and Dohan observed in a cat with experimentally produced diabetes, even of five months' duration, that hydropic degeneration, the incipient diabetic lesion, which had appeared in the island cells, was reversible, and the diabetes could be cured with insulin. Cure in the cat was related to the peculiar persistence, characteristic for that animal, of the hydropic degeneration.

Dohan, Fish and Lukens[6] report two dogs resistant to the injection of anterior-pituitary extract, but following partial pancreatectomy without associated glycosuria, permanent diabetes resulted as soon as a small amount of extract was administered. Two other dogs were made permanently diabetic after sixty-two and ninety-eight days of treatment with small but fairly constant doses of extract. In dogs made diabetic with anterior-pituitary extract, the diabetes may be so severe that 85 per cent or even more of the available glucose of the diet is excreted in the urine, but if these dogs are treated with insulin, the rate of progress of the diabetes seems to be inhibited.

The blood glucose in dogs with moderate and severe pituitary diabetes, sixteen to twenty-four hours after the last feeding, varied widely and showed little relation to the proportion of the available glucose of the food excreted in the urine. It appeared to be a poor index of the severity of the diabetes.

The concentration of serum fatty acids was above normal in the severer cases of diabetes, being particularly marked in dogs excreting 90 per cent of the available glucose of the diet. There was no correlation between the quantity of ketonuria and the concentration of the serum fatty acids in individual determinations. The withdrawal of insulin combined with fat or meat feeding resulted in a marked increase in the concentration of serum fatty acids. The cessation of insulin treatment with fasting was associated with very little change. Meat feeding, in comparison with that of fat, brought about a marked ketogenic effect.

Some animals did not show permanent recovery with insulin treatment. These cases were associated with infections, poor control of the diabetes by insulin or the institution of insulin treatment after more than five months of diabetes.

In last year's review,[3] it was considered that the prevention and cure of the experimental disease were attained primarily by the use of insulin, which permitted rest to the pancreas by the removal of excessive metabolic strain. Subsequently, however, Best and his co-workers[4] not only confirmed the previous observation of Houssay that the hyperglycemic effect of anterior-pituitary extract was not obtained in fasting dogs, but also noted that the feeding of fat had a similar effect in thwarting the action of the diabetogenic factor in the extract. Fasting and the feeding of a high-fat diet are not only reminiscent clinically of the fasting era of diabetic treatment introduced by Allen and of the high-fat diets advocated by Newburg and Marsh in this country and by Petrén in Sweden, but also corroborative of their rational employment as therapeutic agents.

Still more recently, Lukens and Dohan[5] have added another means to the three already known — insulin, fasting and high-fat diet — to be effective in the prevention and cure of experimental diabetes, and with its discovery have afforded an explanation of the action of each of the four. This fourth measure is the use of phlorhizin. Phlorhizin does not decrease the sugar in the urine or indeed the production of sugar, but actually lowers the sugar in the blood by removing it. For the four procedures, a normal — that is, a low — blood sugar represents the greatest common divisor. And here again support is found for the persistent, aggressive and, one might add, orthodox treatment of diabetes originally advocated by Naunyn. We consider the clinical effects of this work far reaching.

Cantilo,[7] in the Argentine, has treated 40 diabetic women in the menopause with large doses of sex hormones, to influence the diabetogenic factor in the pancreas. He considers that he ob tained a constant improvement of the state of all who showed evidence of disturbed hormonal balance, as shown by hyperpituitarism and as measured by the dextrose-tolerance test. He empha-

sizes the need of separating the climacteric from the usual type of diabetes. Successful responses were obtained only with large doses of estrogen and progesterone. Conversely, the use of androgens has been reported as lowering carbohydrate tolerance,[8] and Dr. F. P. Pyles, of Brazil, in a personal communication, refers to a patient whose usual tolerance for 300 gm. carbohydrate was lowered to about 100 gm. while 25 mg. testosterone propionate was being taken.

A pancreatropic as well as diabetogenic factor exists in the anterior portion of the pituitary gland, and it has even been suggested that the former by stimulating the islands to secretion might explain why, in the production of anterior-pituitary diabetes, signs of recovery are repeatedly manifest in the early steps of the injections. Collip[9] has offered evidence on this point, using a primary alcoholic extract of anterior-pituitary tissue. Marks and Young[10] could not confirm his work. Although there is such a factor, they found that it was not identical with prolactin or with gonadotropic, thyrotropic or glycotropic substances. Indeed, they surmise that this principle is not a hormone. Lawrence and Young,[11] by experiments on diabetic human beings and on dogs permanently diabetic with pituitary extract, also failed to confirm Collip's views.

Young[12] attempted to answer the question whether the treatment of an animal with large doses of estrogen would inhibit the liberation from the anterior lobe of the pituitary gland of certain specific hormones and thus influence the course of diabetes. He used dogs made diabetic by injections of anterior-pituitary extract. The administration of large doses of estrone, estriol and diethylstilbestrol to four pituitary diabetic dogs and one that had been depancreatized exerted no obvious antidiabetic action. In fact, with estrone and estriol, the effect was prodiabetic rather than antidiabetic. Young discusses the fact that his results are in disagreement with some earlier results of other authors.

These negative attempts to isolate a pituitary hormone that will offset the diabetogenic pituitary hormone have been failures, but it seems well worth while to continue the search. Haist, Campbell and Best[4] write: "The hope is raised that proliferation without degeneration, produced by the administration of anterior-pituitary extract along with adequate amounts of insulin, may lead to an increase in the islet tissue and a more nearly normal islet fraction." Indeed, Marks and Young[13] have recently shown that certain anterior-lobe extracts increased the insulin content of the rat's pancreas to almost twice normal values.

Encouraged by the reports of the Toronto and Philadelphia laboratories in preventing diabetes in a dog and curing it in a cat, McDaniel, Marble and Joslin[14] reviewed their cases in the hope of finding clinical evidence of prevention or cure. They sought these in the group showing hydropic degeneration of the islands. In human beings, however, fulminating diabetes is infrequent, and it is especially rare to have a fatal case since the introduction of insulin. Warren[15] had only 22 cases of hydropic degeneration among 486 autopsies on patients with diabetes. Eight of these and a later case were from the George F. Baker Clinic. They included 2 patients carefully treated with a relatively or extremely low-carbohydrate diet and insulin who died, we should now say needlessly, of diabetic coma, 1 with coma brought on by hyperthyroidism, 2 in whom cancer entered into the picture, destroying a portion of the pancreas, 3 with infections and 1 with an uncertain duration who died suddenly in coma. Among the cases with a sudden onset, cures were not found in children whose diabetes was not recognized until they were in coma, in prepubertal and adolescent children, in women whose diabetes began in pregnancy or in the menopause, and in the large group of elderly diabetic patients, although some cases of unusual improvement were observed. Yet the search did disclose hints that made the authors urge still more aggressive, active and consistent treatment of the disease with the reduction of carbohydrate and the use of insulin.

Acidosis and Fat Metabolism

Certain recent experiments have discredited four of the former basic concepts of fat metabolism and ketogenesis.

First, Knoop's[16] hypothesis of successive beta oxidation, which he described in 1904, has been discarded, and in its place Hurtley's[17] hypothesis of multiple alternate oxidation of the fatty-acid chain, in which simultaneous oxidation occurs along the entire chain at alternate carbon atoms with the formation of ketones, has been accepted.

Secondly, the ketone bodies, which were formerly considered to be toxic and unavailable for use in the body, have now been shown by Chaikoff and Soskin,[18] Friedemann,[19] Stadie, Zapp and Lukens[20] and others to be the normal end-products of fatty-acid oxidation and to be utilized in the peripheral tissues by both normal and diabetic subjects. It is only when the ketone bodies accumulate owing to the excessively rapid breakdown of the fatty-acid molecules—as in diabetic acidosis, when insulin is inadequate—that the

ketones form more rapidly than they can be utilized and have a toxic effect, because their acidic properties disturb acid-base equilibrium, electrolyte balance and water exchange.

The third revolutionary change is the discarding of the old idea that ketones can be oxidized only by obligatory coupling with carbohydrate oxidation. The experiments of Barker[21] with depancreatized dogs and of others show that fat may be completely oxidized without coupling with carbohydrate oxidation.

The fourth hypothesis — that fatty acids are converted into glucose in the liver — was disproved by the experiments of Stadie, Zapp and Lukens[20] with liver slices of diabetic cats.

At present, Stadie[22] believes that part of or all the fatty acids catabolized undergo a preliminary partial oxidation in the liver to acetoacetic or beta-hydroxybutyric acid. These ketone bodies can be used without chemical coupling with carbohydrate oxidation. He also believes that during exercise the utilization of the ketone bodies keeps pace with their increased formation.

Stadie further believes that the greater the carbohydrate metabolism, the less the fat metabolism.

By actual analysis of total bodies of mice, MacKay and Drury[23] showed that ten times as much of the carbohydrate fed was stored as fat than as glycogen. Fat is ordinarily the great energy reservoir of the body. Drury[24] holds that one of the actions of insulin is to facilitate the formation of fat from carbohydrate and thus to store carbohydrate in its most efficient form.

Treatment

The need for adhering to adequate standards of treatment and control of diabetes is still to be emphasized. Hyperglycemia and glycosuria, as well as acetonuria, are abnormalities that the most seasoned students of diabetes have always sought to correct. As Allen[25] points out, hyperglycemia must denote an insulin deficit, because it is absent in normal persons on identical diets. In the management of diabetes in children, Jackson, Boyd and Smith[26] based their treatment on the premise that physiologic levels of control (normal blood-sugar levels, freedom from glycosuria or insulin shock, and completely adequate diet) are desirable and attainable. It must be admitted, however, that their children remained for comparatively long periods in the hospital. Evidently, in the series of 800 cases described by Smith and Grishaw,[27] standards of treatment and control were orthodox. In a group of 247 obese diabetic patients, the disease was moderately severe in 79 and mild in the remainder, but when reduction in weight was established, the number of moderately severe cases became 32.

Present-day tendencies in dietary treatment seem to be definitely in the direction of moderation with respect to the total amount of carbohydrate fed. Thus, the New England Deaconess Hospital diets containing 140 to 175 gm. of carbohydrate are certainly more commonly used than diets with 200 gm. or more. Our experience has clearly indicated that a smaller dose of insulin is thus required, and that the tendency to hypoglycemic reactions is less. Dr. Allan M. Butler,[28] at the Children's Hospital in Boston, also favors the lower carbohydrate diet and gives an excellent table showing a parallel between the amount of carbohydrate in the diet and the amount of insulin required in diabetic children.

Constancy of Action of Protamine Zinc Insulin

The constancy of the action of protamine zinc insulin is emphasized by Ricketts,[29] who showed that its effect when injected once every twenty-four hours is relatively constant, regardless of the time of day the injection is given. The best criterion for the proper dose is the fasting blood sugar, because protamine zinc insulin metabolizes endogenous carbohydrate. Supplementary crystalline insulin is often necessary before one or two of the daytime meals. Errors in the use of crystalline insulin should never occur, since the only form of crystalline insulin manufactured at present exerts an action that is rapid and comparable with regular insulin, but is not to be compared with the long action of protamine zinc insulin, histone insulin or globulin insulin. In general, most young patients and many with moderately severe diabetes need both crystalline insulin and protamine zinc insulin. A careful comparison of various methods of using these two forms of insulin is given by Watson,[30] and the conclusion is reached that the best results were obtained by the use of two types of insulin, separately injected.

Essential Fructosuria

The importance of essential fructosuria lies in the fact that it is a harmless anomaly of metabolism sometimes mistaken for diabetes and therefore resulting in dietary restriction and the use of insulin in patients in whom neither is required. Lasker[31] has analyzed 40 cases in the literature and added 7 cases of her own. Apparently, this disorder is inherited as a Mendelian recessive, commonly found in the brothers and sisters of patients, but usually absent in the parents. It is essential to remember that fructose may be formed from dextrose in an alkaline urine by the process of chemical inversion. This can happen in a diabetic urine or a urine containing bacteria. Also,

in cases of deficient liver disease, fructose may be excreted in the urine after a test dose of sugar.

Advantages of Early Diagnosis and Aggressive Treatment

The advantages of the early diagnosis and aggressive treatment of diabetes lie in the preservation of a high tolerance. The point is well made by Dr. F. D. W. Lukens, who writes in a personal communication:

> Diabetes has commonly been treated by diet with the least restriction possible, and then by insulin used as late as possible and in the smallest doses possible to control the metabolism. This may be called the principle of minimal treatment. It appears to be fairly suitable for the management of diabetes of long duration, but *at the time of first diagnosis*, at least if soon after onset, a different policy might well be adopted, namely, *early maximal treatment*. The feature underlying this method is that as soon as the diagnosis is made insulin should be given in the largest doses which can be tolerated without reactions. The advantages to be anticipated include: better education of the patient from the beginning; more prompt and complete control of the disease and its progress (by resting the pancreas ?); and the possibility of preventing the condition from becoming permanent. The prevention of permanent damage to the pancreatic islands has not been demonstrated in man, although recent results in two laboratories show that this is possible in early experimental diabetes. It may be that well-equipped clinics will strive for such prevention in human beings albeit with the most sober expectations.

Arteriosclerosis

The coexistence of arteriosclerosis with diabetes, particularly the occurrence of the severe form of occlusive arterial disease in patients in middle life and in diabetes of long duration, is an outstanding problem. Whether the excessive degrees of arteriosclerosis develop prematurely because of uncontrolled diabetes, or whether the tendency is due to an inborn, inherited trait, is still discussed. As a practical problem, it still remains true that the responsibility rests on every physician who treats diabetic patients to give appropriate instruction and treatment to avoid the accidental development of serious lesions, which may often be prevented from reaching a serious stage if early treatment is given. A valuable contribution is a recent account from the laboratory of Dragstedt. Dragstedt and his co-workers[32] found arteriosclerosis of the aorta in 11 depancreatized dogs, an incidence of 13 per cent. In 75 normal dogs, the incidence was 5 per cent. They noted that the dogs were given insufficient amounts of lipocaic to maintain normal fat metabolism, and they pointed to the disturbances of fat metabolism in the liver in diabetes as the mechanism favoring the early and excessive development of arteriosclerosis.

Insulin Resistance

Extraordinary cases of resistance to insulin requiring doses of 1000 to 3000 units a day continue to appear. We[33] have observed two cases — those of a young clergyman and a nurse — in both of which, rather rapidly in the course of a few weeks, such a resistance developed that 2000 units of insulin were required; during the next year, the resistance gradually disappeared. In a case reported by Hart and Vicens,[34] a sixty-year-old Hungarian fruit dealer developed a general, as well as a local, allergic reaction lasting four days after the first dose of insulin. During the next few days, the insulin dose reached the maximum of 920 units. However, the insulin resistance disappeared within a few weeks, and subsequently the patient required no insulin at all.

In certain cases, allergy to insulin requires desensitization. The rapid method of desensitization by the injection every twenty to thirty minutes of very small doses, beginning with 1/100 unit and rapidly working up to several units in the course of four to six hours has been successfully used, but the method we have adopted in several recent cases and prefer has been to begin with 1/1000 unit and increase by 1/1000 unit at each dose before the three meals and on retiring: before breakfast 1/1000 unit, before lunch 2/1000 unit, before the evening meal 3/1000 unit and on retiring 4/1000 unit; occasionally, one can go ahead more rapidly. Patients who begin insulin and then omit it are especially prone to allergic complications.

Another case of severe insulin resistance in a patient with diabetes and chronic lymphatic leukemia is reported by Levi and Friedman.[35] This patient received 4000 units of insulin a day for four days, and 19,900 units over a period of five successive days. His white-cell count varied from 61,000 to 25,000. The possibility that in the large number of leukocytes a trypsinlike ferment was responsible for anti-insulin action was suggested. In a study of carbohydrate metabolism in 4 cases of insulin resistance by Root and Carpenter,[33] it was striking that in 2 cases, when glucose was given to the patient in the fasting state, almost no increase in the respiratory quotient was obtained. Yet with levulose the rise in the respiratory quotient within thirty minutes to an hour was practically equivalent to that found in normal persons. The highly specific character of the metabolic defect is as yet unexplained. In

these 4 cases, the striking feature was the cyclic character of the phase of insulin resistance.

Vitamin Deficiencies

The place of vitamin deficiencies in diabetes continues to excite interest and to stimulate experiments. Brazer and Curtis[36] report a study of 20 patients with juvenile diabetes mellitus, all of whom were found to have poor light adaptation as shown by the Frober–Faybor biophotometer. The daily administration of 60,000 units of vitamin A in the form of fish-liver oil brought about a return to normal, whereas the use of crystalline carotene failed to bring about improvement. In discussing the various causes and explanations of these symptoms, they accepted the inability of the patient with diabetes to convert carotene to vitamin A. This seems to depend on some deficiency in liver function. That there is any specific relation between vitamin deficiencies and the causation of diabetes is still very doubtful. Owens, Wright and Brown[37] have confirmed earlier studies in finding that the administration of ascorbic acid to diabetic patients produced no change in the severity of the diabetes.

The relation of the peripheral neuritis of diabetes to vitamin deficiency is still somewhat uncertain. In a series of 422 ambulant diabetic patients, Fein, Ralli and Jolliffe[38] found 9 who had a symmetrical peripheral neuropathy similar to that found in patients who suffered from proved vitamin B_1 deficiency. The findings that served as a basis for diagnosis consisted in sensory changes in the lower extremities, such as hyperesthesia, tenderness of the calf muscles and loss of position sense and of vibratory sensation, beginning first in the toes and later extending upward, in addition to absence of ankle jerks. The daily administration of thiamine by mouth resulted in cure of 8 subjects and improvement in 1. Some adjustment in the insulin dose went on at the same time, and hence it is possible that diabetic treatment, as well as thiamin, played a part in relieving the condition. Indeed, the exact place of thiamin in the polyneuritis of alcoholism, pregnancy and even beriberi has been questioned by Meiklejohn.[39] He points out that the laboratory animals suffering from thiamin deficiency do not have a true peripheral neuritis but do have a disturbance of the metabolism of the central nervous system. His belief is that, when a true peripheral neuritis occurs, the treatment should include an ample and nutritious diet together with the administration of yeast and crude liver extract to ensure an adequate supply of vitamin B complex. In the treatment of the neuritides associated with diabetes, when a vitamin deficiency is suspected, it is probably wise to use the complete vitamin B complex rather than thiamin alone.

One of the features of diabetic neuritis is the existence of an increased amount of protein in the cerebrospinal fluid without an increase in cells. This condition is characteristic of the Guillain–Barré syndrome or polyradiculoneuritis. A series of 15 cases of this type is described by de Jong.[40] In these cases, the total protein in the acute stage varied between 125 and 412 mg., with an average of 214 mg. for 100 cc. The average cell count was 6. The patients were quite young, the average being twenty-two years. The onset was rather sudden, and recovery occurred usually after an average of eight weeks. Slight infections had been present at the beginning in some cases. These cases differed materially from the diabetic cases that one sees clinically. Ordinarily, in diabetic patients, the onset is insidious, and in a fully developed case a young person's recovery frequently requires more than eight weeks. However, in severe cases, development of atrophy and contractures and a long duration of the neuritis were signs akin to what we see in diabetic patients. The fatal cases had bulbar involvement and respiratory failure.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27371

PRESENTATION OF CASE

A fifty-nine-year-old woman came under medical observation with the following story.

Twenty years previously, the patient had been treated for peptic ulcer, without recurrence of symptoms, and about this time she suffered a transient attack of thyrotoxicosis, which was treated with x-rays. The details of the latter illness were not available. Ten years later at the time of the menopause, she became mentally unstable, with symptoms referable to the gastrointestinal tract and heart and "a good deal of jointiness." For this illness, she visited several sanatoriums. Six years before, the patient had suffered from regurgitation of food shortly after eating, and at this time it was found that the heart was enlarged and that the liver extended two fingerbreadths below the costal margin; the latter was not tender, and the upper border reached the fifth rib. X-ray studies revealed a slightly enlarged heart and tortuous esophageal folds, with some delay at the cardia, but no varices could be demonstrated. The basal metabolic rate was +13 per cent. Approximately one year later, the patient suffered a transient attack of pleurisy, and for twenty-four hours a left pleural friction rub was audible. She carried on in fair health for four years, and during this time she was considered by successive physicians to be a neurotic patient whose regurgitation of food was not based on organic esophageal disease. Her insistence that she had heart trouble was denied by all. She complained of a good deal of "jointiness" in her hands, and these symptoms were thought to be due to degenerative arthritis, with hypertrophic changes at the joint margins, but no x-ray films were taken to prove this point.

However, for the summers of the previous three years, she had had "mosquito bites" which developed on the dorsal surfaces of the forearms, the jaw line of the face, and along the collar line near the sternoclavicular junctions. These lesions began as tiny, reddish, slightly elevated areas on which there soon developed a central scab. They itched, and the scab pulled off when scratched, leaving a small pit. The erythematous area widened to about the size of a dime, or even a quarter, with a large necrotic area in the middle. These lesions disappeared in the course of four to six weeks, leaving a depressed white scar, with punctate areas in the scar that probably represented the site of hair follicles. Sometimes at the end of this period, after feeling somewhat giddy for several days, the patient suddenly developed "a lump between her breasts," and a sense of pressure aggravated by breathing and by lying flat or on the left side. This symptom was accompanied by mild nausea and inability to relax, and precluded sleep. It disappeared by morning but recurred the next day for a few hours. The patient had also noticed some shortness of breath on exertion. She had lost 15 pounds, and there was a stare to the eyes, with lidlag. The left border of the heart was 10 cm. from the mid-line in the fifth left interspace, and the first sound was described as "mushy," with a shuffling systolic blowing murmur. The heart beat was regular at a rate of 70, the pulmonic second sound being greater than the aortic, and at the lower sternum a scratchy sound was heard in systole that was believed to be extracardiac; the blood pressure was 144 systolic, 85 diastolic. The liver was palpable two fingerbreadths below the costal margin on deep inspiration, with its upper border at the fifth rib. Neurologic examination was negative. The skin lesions were present, but only in the form of depressed atrophic scars, no fresh lesions being noticed. The patient ran a low-grade fever for one week. X-ray films of the colon and gall bladder, as well as a Graham test, were negative; at the lower end of the esophagus a delay in passage of the barium was noted, with possibly some thickening of the mucous membrane, but it was not the picture of cardiospasm or cancer. Degenerative changes were present about the joints. An electrocardiogram revealed moderate left-axis deviation, with T-wave changes that were possibly due to digitalis or a combination of digitalis and coronary disease. The basal metabolic rate was +34 per cent.

A month later, repeated readings of the basal metabolic rate gave figures of +28, +39 and +36 per cent, so that the patient was given iodine, and in a few weeks the reading was +17 per cent. There was no palpable goiter or evidence of a substernal gland by x-ray examination. Blood counts were normal, the sedimentation rate was high normal, and the stools were normal. The patient carried on for the next four months, gained 7 pounds and remained mentally well; she had very little regurgitation of food, but there was still some exertional dyspnea. At the end of this period, a sensation of weight developed in the anterior chest, and shortness of breath increased. On examination, she did not appear ill, but a to-and-fro

friction rub was heard over the precordium, base and apex, loudest over the left sternal border at the fourth interspace. The heart was regular at a rate of 96, with the same systolic murmur, and the pulmonic second sound was greater than the aortic; the blood pressure was 130 systolic, 90 diastolic. The liver was three fingerbreadths below the costal margin. The white-cell count was 8000, and the sedimentation rate 40 mm. in one hour. An electrocardiographic recording showed marked left-axis deviation, a PR interval of 0.22 second and a QRS complex of .09 second; T_1 and T_2 were upright, T_3 inverted, and T_4 flat. The temperature had risen to 100°F. forty-eight hours later, but fell to normal in the next two days, and by this time the precordial friction rub had disappeared. The patient was kept in bed for one month, then gradually allowed up, but it was noted that the neck veins were distorted in recumbency, that there was an increase in dyspnea, and that a nonproductive cough occurred after meals and when the patient was lying in bed. She went to the country at this time, and within a week or two began to develop the aforementioned erythematous skin lesions. The patient's condition remained essentially unchanged for the next two months, at the end of which a rolling heave was observed over the precordium, which was transmitted to the liver region. The liver reached a point five fingerbreadths below the costal margin, but was not tender; the spleen could not be felt, nor were there other signs of congestive failure. Examination of the urine and blood was negative. Salyrgan produced a diuresis, but did not appreciably affect the exertional dyspnea or cough. A few weeks later, crackles were audible at the lung bases, more pronounced on the left; there was no visible or palpable pulsation of the liver.

On examination, the patient was well developed and well nourished, tired and weak, but mentally clear, with moderate exertional dyspnea; however, she appeared only slightly ill, and the temperature was normal. The cervical veins were distended; there was slight exophthalmos, but the thyroid gland was not enlarged. The fingers were thick and shiny, and the skin showed many small white scars and a few fresh, reddish, scabbed maculopapules on the hands, forearms, face and anterior neck. Examination of the heart showed enlargement to the left, with a normal rhythm at a rate of 80 and a bifid apical impulse. The pulmonic second sound was greater than the aortic, and there was a diastolic murmur at the apex and lower end of the sternum. The pulse was normal, the arterial walls soft, and the blood pressure 140 systolic, 95 diastolic. Persistent fine rales were present at both lung bases, but no dullness. The liver was enlarged and tender, reaching four fingerbreadths below the costal margin; there was no peripheral edema. Examination of the urine and blood was negative. An electrocardiographic recording showed a normal rhythm at a rate of 80, and a PR interval of 0.24 second; there were low voltage of the QRS waves, flattish T waves and a deeply inverted T_4.

The patient was confined to bed and given vitamins, digitalis, weekly mercurial diuretics, a normal diet and limited fluids. She improved, but cardiac reserve hung in the balance, with gallop rhythm at the apex, pronounced accentuation of the pulmonic second sound and jugular pulsation. During the next few weeks, the patient had less respiratory difficulty and gained in strength, but new umbilicated papules appeared on the face and arms, edema of the legs developed, and the liver was palpable at the umbilicus. At the end of seven weeks, a protodiastolic gallop was heard maximally at the lower end of the sternum, and there were rales at the lung bases; the liver was firm and slightly tender, and had receded to the costal margin; new skin lesions appeared, the older ones becoming scarred. The urine contained an occasional hyaline cast with a trace of albumin; the blood was normal, with a sedimentation rate of 30 mm. in one hour. Within three weeks the patient began to lose ground appreciably; she developed anorexia, cough, increasing dyspnea and arthritis of the finger joints, and the temperature rose to 101°F. On examination, the fingers were spindled, and new skin lesions were present on the face, arms and legs. The heart findings were unchanged, rales were present at both lung bases, and the liver again reached the umbilicus. Gradually, edema increased in severity and grew more widespread, involving the hands and face; no longer was there response to mercurial diuretics, and jugular pulsation was visible to the ears. The patient became weak, her hands and feet were cold and purple, and the pulse was rapid and feeble; the temperature dropped to 95°F., and albuminuria increased. Occasionally, a curiously loud first or second heart sound could be picked up. Fresh pruritic skin lesions continued to develop and appeared as raised, gray-white, dry, scaly areas measuring up to 4 mm. in diameter and surrounded by purplish margins, the whole averaging 1 cm. in diameter.

Terminally, there was little stupor, and death occurred quite suddenly, with deepening cyanosis, approximately six years after the discovery of cardiac enlargement. Fever was present almost daily for the last five months of life.

Differential Diagnosis

Dr. Walter Bauer: Being, as Dr. Mallory knows, extremely interested in lupus erythematosus disseminatus I find it very difficult to get away from a diagnosis of that disease in this case. True, the patient was somewhat older than such patients usually are. However, we know it does occur at this age. Over a six-year period, this patient suffered from pericarditis, pleurisy, a recurring rash and, finally, arthritis. It is very difficult to say what caused the joint symptoms. They may have been due to degenerative joint disease. I believe that the patient suffered from mediastinopericarditis rather than simple pericarditis. The former is rare in disseminated lupus, but there are on record three cases that have had a well-defined mediastinopericarditis. There is no mention made in this record of whether she had a paradoxical pulse.

Dr. Myles P. Baker: She did not.

Dr. Bauer: Or whether the heart was fixed in position.

Dr. Baker: It was not.

Dr. Bauer: And there is also no mention whether x-ray study showed anything but upward displacement on inspiration.

Dr. Baker: That was not looked for.

Dr. Bauer: One wonders if the first episodes in this patient's history could not be accounted for on the basis of the same disease. I took the liberty to ask Dr. Aubrey O. Hampton whether the x-ray findings in the esophagus could be accounted for on the basis of mediastinitis. He stated that he did not know. In mediastinitis, "a rolling" of the esophagus is usually observed. I do not know whether the esophagus in this case showed such changes.

Dr. Baker: I should say not.

Dr. Bauer: Dr. Hampton said there was nothing about the x-ray picture to lead one to suspect cardiospasm or intrinsic disease of the esophagus. This patient never had a Broadbent sign?

Dr. Baker: No.

Dr. Bauer: One would think she would have had distention of the neck veins as the disease progressed.

Dr. Baker: I did not look for that.

Dr. Bauer: The pleurisy could, of course, have been a manifestation of disseminated lupus. The recurrent rash each summer is very suggestive of disseminated lupus. There is one case on record of a patient who had recurring skin rash every summer for ten years except one and that was the year when he worked nights instead of days. There is another case on record of recurring skin rash for four successive summers, with complete disappearance in between. Another point in favor of this diagnosis is the fact that some of the skin lesions left scars. The arthritis that developed terminally could have been a manifestation of the disease. Whether the original joint symptoms were related to this final illness, one cannot say. One might ask if it is not unusual to see pericarditis as the first sign of the disease. The answer is that it is unusual. However, visceral manifestations may be the first evidence of the disease, and we have seen one patient who had chronic crippling arthritis for ten or twelve years before developing skin lesions. Another had chronic arthritis for a period of four or six years before visceral symptoms became evident. Many of the classic findings may be absent. I think the distribution of the skin lesions in this case is consistent with the diagnosis. The patient had no evidence of the bone-marrow involvement that is sometimes seen in this disease, nor did she exhibit purpura. The absence of leukopenia should not disturb us, because only 30 per cent of our 65 cases had low leukocyte counts.

The patient never developed hypertension. The terminal urinary findings could be explained on the basis of mediastinopericarditis, which I believe she had. Should one consider the possibility of pericarditis from other causes? Did she have Pick's disease of tuberculous origin? One could explain the skin lesions, which resulted in scarring, on the basis of tuberculosis. It would, however, be extremely difficult to explain the arthritis in this manner.

One must mention periarteritis nodosa. It commonly causes pericarditis, which may be associated with mediastinitis. Some of the other findings observed in this case would not be so readily explained by this diagnosis, although we must admit that an additional case of periarteritis nodosa could have all the findings presented by this patient, including the arthritis. We have seen one patient with periarteritis nodosa with a marked synovitis. In this case, the typical vascular lesions of periarteritis nodosa were demonstrated in the synovial blood vessels. A primary vascular disease such as periarteritis nodosa of six years' duration would probably have affected the vessels of the pericardium, heart, cerebrum, abdomen or legs at some time during the course of the disease.

One might suspect rheumatic fever. The PR interval was prolonged — 0.22 and, finally, 0.24 second. However, the skin lesions were not those of rheumatic fever. Rheumatoid arthritis can involve serous surfaces, but there seems little reason for seriously considering it in this case.

I consider disseminated lupus the best explana-

tion of this patient's symptoms and physical findings. One might argue that mediastinal involvement is not in keeping with this diagnosis. However, I know it can occur. Therefore, I believe we were dealing with a patient whose mediastinopericarditis was part and parcel of the picture of disseminated lupus. Tuberculosis need not be seriously considered. Although periarteritis nodosa is a distinct possibility, I believe we can exclude it.

DR. TRACY B. MALLORY: Does anyone care to hazard a diagnosis or express an opinion?

DR. BAKER: This woman presented the picture terminally — indeed, during the last five months — of febrile illness and progressive right-sided heart failure, with accentuation of the pulmonic second sound, a finding that was difficult to explain. We believed that she had disseminated lupus, and in retrospect I doubt very much that she had a thyrotoxicosis. She had always had prominent eyes, with lidlag. I think that an elevation of the basal metabolic rate has been noted in disseminated lupus, presumably in a case in which fever was not prominent. I suspect we were on the wrong track in attributing an elevated basal metabolic rate to recurrent thyrotoxicosis. The difficulty as I saw her from day to day was how to explain the right-sided heart failure that was obviously taking her to her end. I could find no reference in the literature of disseminated lupus to right-sided heart failure, no definite description of myocardial disease that would account for such a picture. We considered the accentuated pulmonic second sound — the loudest heart sound — as evidence of chronic cor pulmonale.

DR. EDWARD F. BLAND: One could explain that with mediastinopericarditis.

DR. BAKER: But would one expect the meager heart sounds and the pronounced gallop rhythm?

DR. BLAND: I do not see why they need be anything more than evidence of a failing heart.

DR. BAUER: I do not see why an accentuated pulmonic second sound must necessarily be indicative of right-sided heart failure. Was she a slender person?

DR. BAKER: No, she was not.

DR. BLAND: I should be inclined to discount the finding.

DR. BAKER: What of the gallop rhythm?

DR. BLAND: It is a good sign of weakened myocardium, either on the right or left.

CLINICAL DIAGNOSES

Acute disseminated erythematosus.
Cardiac failure.

DR. BAUER'S DIAGNOSIS

Lupus erythematosus disseminatus.

ANATOMICAL DIAGNOSES

Disseminated lupus erythematosus (probable).
Idiopathic pulmonary endarteritis (Ayerza's disease).
? Periarteritis nodosa of pulmonary vessels.
Polyserositis: pericarditis, pleuritis, peritonitis.
Cor pulmonale.
Infarcts of lungs.
Healed pyelonephritis, slight.
Arteriosclerosis, aortic and coronary.
Lymphadenopathy, axillary.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed a polyserositis. There was turbid fluid in one pleural cavity. There were some old but loose adhesions and some extensive fluid in the pericardium, and there was 150 cc. of turbid fluid — a small amount — in the pelvic portion of the peritoneal cavity. The heart was hypertrophied, weighing 450 gm., but all the hypertrophy was on the right side, an extreme grade of cor pulmonale. The right ventricle measured from 7 to 10 mm. in thickness, and since it was also markedly dilated, that represents as marked hypertrophy of the right ventricle as I have ever seen.

DR. BAUER: The patient had left-axis deviation, according to the electrocardiogram.

DR. MALLORY: I am sorry about that, but I have no explanation to offer. The lungs were fixed whole by injection of formalin into the bronchial tree. Later, they were examined by means of numerous cross-sections. When the surfaces of these sections were examined under the dissecting microscope, it was apparent that every small artery was markedly thickened, many having no visible lumen, whereas the large arteries showed numerous and large plaques of atheroma. On microscopic examination, we found ordinary but severe atheroma of the large and intermediate-sized pulmonary arteries and more puzzling changes in the pulmonary arterioles. In many places, this was a fibrous intimal thickening, sometimes evidently the result of thrombosis, organization and recanalization. In some arteries, fresh thrombi were still apparent. In others, the picture was more suggestive of an endarteritis. However, there were a significant number of vessels in the lungs in which the picture was still different. The media of these arteries was thick and necrotic. There was a periarterial granulomatous process with polymorphonuclears and numerous monocytes, and the picture in these vessels was indistinguishable from periarteritis nodosa.

So far as the rest of the body is concerned, not a diseased arteriole was found, except for some

ordinary atheromatous changes in the heart and in the uterine vessels. The spleen was normal in size. The liver was considerably enlarged and deeply congested, with some central necrosis. The kidneys weighed 350 gm., a little larger than normal. There were a few patches of sclerosed glomeruli, a few dilated tubules filled with hyaline casts and a few lymphocytes suggestive of a very mild healed pyelonephritis. There were also, I think, a few glomeruli showing focal glomerulitis. Whether one could separate those entirely from the old pyelonephritis and attribute them to another process, I am not sure.

Most of the lymph nodes of the body were not enlarged. On external palpation, we did not feel any, but on dissecting into the axillas, we found on both sides a great many enlarged nodes, wet, pink and highly vascular. On microscopic examination, they showed great increase in blood vessels, and necrosis of the germinal centers, changes that we usually find in acute disseminated lupus.

Although a few vessels in the lung were characteristic of periarteritis nodosa, nothing else in the body favored that diagnosis; there were a number of clinical and a few anatomic points that fit better with the diagnosis of lupus.

CASE 27372

Presentation of Case

An eighteen-year-old single primipara was referred to the hospital three weeks after delivery.

Two months before admission, the patient presented herself at the prenatal clinic of another hospital, where her condition was followed until the time of delivery. She had no untoward symptoms, and physical examination revealed nothing abnormal except minimal ankle edema; the blood pressure was 100 systolic, 80 diastolic, and the urine was normal. During the last six weeks of pregnancy, she gained 11 pounds, and at the time of the delivery was recovering from a cold. Three weeks before admission to this hospital, her child was born after a normal six-and-a-half-hour labor aided by an episiotomy, although it was stated that the patient lost slightly more blood than is usual. On the second post-partum day, the ankle edema was the same, but the face became pallid and puffy. The blood showed a red-cell count of 2,400,000 with a hemoglobin of 48 per cent, and a white-cell count of 16,000 with a normal differential. A Fouchet test was negative. The blood pressure was 100 systolic, 64 diastolic, and the urine was normal. The next day, edema was more marked, and the liver was palpable two fingerbreadths below the costal margin and was somewhat tender. A catheter specimen of urine was strongly positive for albumin, had a specific gravity of 1.015 and contained many white blood cells; colon bacilli were cultured. The nonprotein nitrogen of the blood serum was 100 mg., the uric acid 14 mg., the cholesterol 181 mg., and the sugar 69 mg. per 100 cc.; the icteric index was 5. On the third and fifth post-partum days, transfusions of 500 cc. of blood were given. On two occasions intravenous injections of 100 cc. of 50 per cent glucose were given for anuria. The urine volume rose from less than 400 cc. to more than 1000 cc. The fluid intake was forced to 2000 cc., and the edema increased. At no time did the temperature rise above 99°F. During the eight days before admission, the white-cell count dropped from 35,000 to 21,000. The lochia was foul and persistent, but the uterus was said to have involuted satisfactorily with the aid of two courses of Ergotrate. Finally a small mass developed just lateral to the umbilicus between the lower edge of the liver and the fundus. The edema had slowly increased.

Four months before admission, the patient was in bed for five days with tonsillitis. Her physician painted her throat, and recovery was satisfactory. There was a history of occasional nocturia of several years' duration. The patient's menstrual periods had always been normal. The family history was irrelevant.

On examination, the patient responded slowly and was cyanotic and orthopneic. There was pitting edema of the entire body. She preferred to lie on her right side, her breath coming in shallow gasps, with occasional coughing. The tongue was dry, and there were sordes on her lips. The left arm was much smaller than the right and showed a large ecchymosis above the elbow. The trachea was slightly deviated to the left. Examination of the lungs revealed dullness, increased vocal fremitus and bronchial breathing over the entire right chest. Slight dullness was present at the left base, but the breath sounds were vesicular, with no rales. Examination of the heart showed the left border to be 1 cm. to the left of the mid-clavicular line. The sounds were somewhat distant, with occasional extrasystoles and an inconstant gallop rhythm; the blood pressure was 90 systolic, 68 diastolic. The abdomen was distended and edematous, and shifting dullness was present. The liver was palpable three fingerbreadths below the costal margin. The fundus of the uterus reached a point 3 cm. above the symphysis pubis. Pelvic examination revealed a septic perineorrhaphy, oozing pus. The uterus was in second-degree retroversion, enlarged and slightly fixed. The vaults

were clear. The pupils were dilated, but reacted to light and accommodation. The fundal vessels showed slight narrowing. Examination of the nervous system was negative.

The temperature was 102°F., the pulse 90, and the respirations 30.

Examination of the urine showed a specific gravity of 1.026 and a ++ test for albumin; the sediment was "loaded" with white blood cells and contained an occasional granular cast. A culture grew abundant colon bacilli. Examination of the blood showed a red-cell count of 5,000,000 with a hemoglobin of 13.5 gm. (photoelectric-cell technic), and a white-cell count of 21,000, with 82 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 63 mg. and the serum protein 4.6 gm. per 100 cc.; the chlorides were 91.4 milliequiv. and the carbon dioxide combining power 16.5 milliequiv. per liter. A serum van den Bergh was biphasic and slightly above normal. A vaginal smear was negative for beta-hemolytic streptococci; a throat swab showed a few colonies of beta-hemolytic streptococci.

An x-ray film of the chest showed a large amount of fluid on the right side and less fluid on the left. The outlines of the diaphragm and heart were obliterated by the fluid. Nothing could be said about the size of the heart or the condition of the lungs. A flat abdominal film showed marked enlargement of the soft tissues of the abdominal wall, consistent with edema. The psoas shadows were poorly outlined, the kidneys incompletely visible. There was an unusual stripy appearance of the abdomen, perhaps due to edema in the retroperitoneal tissues, which accounted for the poor demonstration of the kidney and psoas shadows.

An electrocardiographic recording showed normal rhythm, with a rate of 90 and a PR interval of 0.15 second. T_1 was flat to inverted; T_2 and T_3 were inverted. There was slurring but no abnormality of the QRS complex.

On the day of admission, the right chest was tapped on two occasions, and yielded 250 cc. and 800 cc. of slightly cloudy, straw-colored fluid. This fluid had a specific gravity of 1.011, contained 3300 red blood cells and 58 white blood cells per cubic millimeter, clotted in five minutes on standing, and yielded no growth. After this procedure, the patient was more comfortable. On the second hospital day, the temperature was 100.5°F., the white-cell count 12,000, and the blood pressure 100 systolic, 60 diastolic. An electrocardiogram showed auricular premature beats with a rate of 85 to 90 and a PR interval of 0.19 second. There was slurring of the QRS complex and moderate right-axis deviation. T_2 was diphasic, T_3 inverted. The next day, the patient was placed in an oxygen tent, remained uncomfortable, but was apparently holding ground. The blood pressure dropped to 70 systolic, 45 diastolic. Despite five blood transfusions of 500 cc. each and general supportive measures, the patient rapidly failed, with steadily increasing edema, cyanosis and dyspnea. Death occurred on the sixth hospital day.

Differential Diagnosis

Dr. Fuller Albright: "A Fouchet test was negative," whatever that is.

Dr. Tracy B. Mallory: The reagent is a mixture of trichloracetic acid and ferric chloride, which is a strong oxidizing agent and turns bilirubin green. The test is usually applied to urine.

Dr. Albright: I should like to be sure that the urine was normal in all other respects on the second post-partum day. If so, it would rule out many things. One must always remember that specimens can be mixed.

The fact that the liver was apparently enlarged is not particularly significant because of the relaxed abdominal wall from the recent pregnancy.

The anemia was controlled by transfusions.

"A throat swab showed a few colonies of beta-hemolytic streptococci." It would be much more interesting to know whether it was negative for pneumococcus.

I have listed seven things that I shall consider, but only the last two do I consider very seriously. The first is post-partum eclampsia. The patient did not have hypertension. I do not think it was eclampsia. The second thing is a colon-bacillus pyelonephritis. She was sick on the second day after delivery, and the urine was said to be normal at that time. If that was true, she was not sick because of pyelonephritis. Besides, there is not so much albumin in the urine with pyelonephritis, and her course was much too rapidly downhill for uncomplicated pyelonephritis, and I rule it out as the primary disease. I do not believe that she died of colon-bacillus pyelonephritis or septicemia. The next possibility is pneumococcal pelvic infection, with secondary nephrosis, for which one can make a fairly good story. Again, if the urine was normal on the second post-partum day, it would rule out this diagnosis. The patient did have the nephrotic syndrome — at least, a great deal of albumin, a low serum protein with ascites, fluid in the chest and generalized pitting edema. Accordingly, one can make a fairly good story for pneumococcal infection somewhere, leading to nephrosis and ending with a gradual "petering-out." It is too bad that we do not know

whether there were pneumococci in the culture. The fourth condition is acute glomerulonephritis. That was apparently considered also by the person who took care of the patient. I think we can rule it out. There were no red cells in the urine, and the rest of the picture was not particularly characteristic. Then one comes to the question, Did she have a cardiac condition? In favor of that was the enlarged liver. She had a certain amount of edema, a gallop rhythm and a fall in blood pressure, and one wonders if she had massive pulmonary infarcts, with a failing right ventricle. She did have right-axis deviation at one stage, but I do not believe that she had massive pulmonary emboli. There was no particular etiology for cardiac disease. She might have had pericarditis as the cause of the electrocardiographic changes, but that was probably not the diagnosis. The electrocardiographic changes can be explained by the edema of the skin, and do not necessarily indicate cardiac disease. I shall say that the patient did not have, primarily, cardiac disease. I do not believe they would have given the case to me if she had had. One of the more probable diagnoses is a hepatitis of some kind. People do get liver disease after pregnancy. She did have an expanding liver, and a peculiar mass on the right (?) side. She had a low serum protein, which would go with it, and a strange sort of exit, which does not show on the chart. She died with a fairly normal-looking chart, as so many patients with severe liver disease do, but the serum van den Bergh was not impressive, nor was there enough bilirubinuria for hepatitis. I do not believe that she died of toxic hepatitis. That is a diagnosis one might consider more seriously, however. The ecchymosis may have been indicative of vitamin K deficiency and severe liver disease.

The one diagnosis I really am hoping it may turn out to be is terribly far fetched. We know that patients who have severe hemorrhages at the time of delivery and who go into shock are prone to develop infarcts of the pituitary glands and resulting Simmonds's cachexia. We have had three such patients in the Ovarian Dysfunction Clinic. Could this patient have had this? From her red-cell count, it is apparent that she lost a large amount of blood at the time of delivery, following which she ran a rapidly downhill course. The blood chemical findings were quite extraordinary, and I think more attention should have been paid to them in the treatment. Both the serum chloride and the serum carbon dioxide combining power were lowered, each by about 10 milliequiv. per liter. Since these are both anions, and since the sum of the anions in the serum equals the sum of the cations, we can infer either that the patient had an accumulation of some other anions in her serum or else that her cations were correspondingly low. The most likely possibility is that she had a low serum sodium. This would suggest an adrenal insufficiency or possibly adrenal insufficiency secondary to pituitary disease, that is, Simmonds's cachexia. Of course, the high nonprotein nitrogen and the high uric acid fit in with acute adrenal failure. Against the diagnosis of pituitary infarct, of course, is the general anasarca. I never heard of a patient with Addison's disease or Simmonds's disease who had general anasarca.

In conclusion, if the patient has any endocrine disease, I believe it is Simmonds's cachexia, with a terminal urinary infection. My second choice is liver disease. My third choice is pneumococcal infection with nephrosis.

DR. MALLORY: Are there any other suggestions?

DR. PAUL D. WHITE: May I say a word about the electrocardiogram? I think it is unlikely that edema alone would have such a preponderant influence on the T waves. It may have a striking influence on the total voltage of both QRS and T waves, but there are possible factors behind the edema such as renal or adrenal insufficiency that could change the T waves to this degree without necessarily any intrinsic heart disease or blaming the anasarca. What do you think, Dr. Sprague?

DR. HOWARD B. SPRAGUE: I wondered why the right-axis deviation developed.

DR. WHITE: That was only on the first occasion and was slight.

CLINICAL DIAGNOSIS

Acute glomerular nephritis with edema.

DR. ALBRIGHT'S DIAGNOSES

Pituitary infarct, with Simmonds's cachexia.
Terminal urinary infection.

ANATOMICAL DIAGNOSES

Acute pyelonephritis.
Nephrosis?
Thrombophlebitis of uterine veins.
Multiple pulmonary infarcts.
Septic thrombosis of right auricle.
Anasarca.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Dr. Albright is safe in one regard, I am sorry to say, because the pituitary

gland was not examined, so that I can rule Simmonds's disease neither in nor out. We did, however, find a good deal wrong in various other organs. The most striking lesions were in the kidneys, which were considerably enlarged, and contained multiple small abscesses especially numerous in the left kidney. The pelvis of the left kidney was inflamed, and there was also a severe hemorrhagic cystitis. The question might be raised whether it was a hematogenous infection or a retrograde infection. I should say that it was definitely hematogenous, but the process still lies within the group of processes that we lump together as pyelonephritis. The theory of retrograde infection has rather disappeared in recent years, and we consider the vast majority of these cases to be hematogenous. The next question to come up is whether there was anything besides pyelonephritis. The glomeruli were perfectly normal. The tubules showed a very distinct swelling of the tubular epithelium and the presence of enlarged albuminous granules. The picture is not much beyond what is ordinarily called cloudy swelling, which may be found as the terminal stage of many febrile illnesses, but on the other hand, it is perhaps just a little bit beyond it and one might be justified in suspecting a nephrosis. If so, it was considerably masked by the severe pyelonephritis.

The right auricle contained a thrombus that appeared septic, both grossly and microscopically. The condition could be called, I think, an auricular endocarditis if one wished. The direct smears and cultures, however, failed to show organisms or growth. Thrombi in the uterine veins also suggested sepsis. There was massive edema, and each pleural cavity contained over a liter of fluid. There was 150 cc. of fluid in the pericardium. The abdomen contained considerable ascitic fluid. The liver was not enlarged, weighing only 1300 gm., and this again is an example of a rather small liver readily felt in a patient who has ascites.

Dr. White: Was the pleural fluid clear?

Dr. Mallory: Yes; the lungs were also very wet.

Dr. White: Did the myocardium show any involvement?

Dr. Mallory: Not that of the ventricles. Beneath the septic thrombus in the auricle, there was some inflammation.

A Physician: What was the mass described in the clinical findings?

Dr. Mallory: It may have been the gall bladder, the wall of which was edematous and thickened. Nothing else was found to account for it.

Dr. Albright: What was the cause of death?

Dr. Mallory: I think it is difficult to be sure of the mechanism of death. I should be inclined to think it was respiratory embarrassment from large amounts of pleural fluid and pulmonary edema. The patient certainly had infection too, but cyanosis was spoken of repeatedly in the course of the record.

Dr. Bernard M. Jacobson: Do you think it was a fairly acute pyelonephritis coming on a few weeks before delivery?

Dr. Mallory: I should have to guess from the autopsy findings that the pyelonephritis was the chief cause of death. I cannot rule out the possibility of some degree of nephrosis as well, but I should like to make one diagnosis, and that would be pyelonephritis.

Dr. Robert E. Glendy: Were there abscesses in any of the other organs?

Dr. Mallory: No.

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THE ROSE OF NO MAN'S LAND

FOR two years, we have been told how different this war is, but as we prepare to defend ourselves and as we watch the British facing its realities, we realize that some of the alleged differences have been purely imaginary. One of the most wishful thoughts has been that man power would not be needed — that this was to be a war of machines. In certain branches, this may be partly so, but in the medical services it is not. One after another, we see the familiar lacks and inadequacies facing us again. It makes little difference whether a man is wounded on a battlefield or in a wheat field or at his desk or in his bed — he must be the recipient of the very best medical and surgical care that can be devised under the circumstances. Preserved blood and serums may replace gum acacia and salt solutions, and tetanus toxoids may replace antitoxins, but medical and surgical services will be more than ever in demand.

It is thus not surprising that the nurse — dramatized in the other war as the "rose of no man's land" — is again coming into such demand that she must soon be vigorously recruited if our national supply is not to fail us in the coming crises. Fifty thousand well-educated young women have already been called for by the Surgeon General of the United States Public Health Service to avert "serious damage to the Nation's health during the present emergency." These young women, by entering the already established schools of nursing in our civilian hospitals, — particularly if they are well educated, — can soon relieve staff nurses who are already fully trained and who are already in demand, at least for the nurse-corps reserves of the United States Army and Navy.

In addition to enrolling approximately 600 reserve nurses per month, the Army at the present time has nearly 6000 nurses on active duty and anticipates an authorized quota of 8237 nurses for the fiscal year of 1942. The Surgeon General of the Navy has stated: "The Navy Nurse Corps has now approximately 700 nurses on active duty, including nearly 140 reserve nurses. There are more than 1000 reserve nurses awaiting a call to duty, and this number may be increased by an additional thousand or more by the end of the year." Practically all such nurses must come from those now in civilian nursing duties, and it can accordingly be seen just where the shoe is going to pinch.

If we are to keep abreast of military and civilian nursing requirements, these 50,000 young women must be enrolled for the fall term in accredited schools of nursing. Surgeon General Parran has stated, "An especial effort should be made to enlist the interest of young college women in this important field, inasmuch as the greatest demand is for nurses who have had a superior education." Under Dr. Parran's direction, the States Relations Division of the United States Public Health Service is administering a recent congressional appropriation of $1,250,000, which will facilitate the

training of additional nurses, presumably in the schools of nursing already established and accredited.

Even more than in the last war, young women as well as young men are actively challenged. Again, we begin to visualize some of the difficulties to be faced by those who will be charged with keeping "the home fires burning," for the depletion of our civilian nursing services is inevitable. Energetic action to recruit nurse trainees on an emergency and patriotic basis is in order *now*. If the use of machines — x-ray, electrocardiographic and so forth — is doubled in the medical and surgical services of this war, the use of man power and woman power must be tripled.

SALVATION ARMY APPEAL

The Greater Boston Annual Maintenance Appeal of the Salvation Army will begin on September 16 with a dinner at the New England Conservatory of Music. Scores of volunteer leaders and workers will assist in raising the $200,000 that is the goal for 1941–1942.

In the corps cities of Cambridge, Chelsea, Everett, Malden, Medford and Somerville, separate campaigns will be directed to collect the amount set for this year. The quota assigned to the thirty-two towns in which the Salvation Army does not conduct corps organizations is $40,000.

The Salvation Army, which maintains more than thirty institutions that care for the needy, merits the support of all members of the community. It is hoped that physicians in particular will respond generously, as they have in previous years, to this appeal for help.

MEDICAL EPONYM

Kahn Test

The precipitation test for syphilis that has attained the widest use in this country is that proposed by R. L. Kahn (b. 1887), of the Michigan Department of Health, in his paper, "Simple Quantitative Precipitation Reaction for Syphilis," which appeared in the *Archives of Dermatology and Syphilology* (**5:** 570–578, 1922). The author's test has been modified and discussion of it amplified in numerous later papers and a book.

> The precipitation method proposed in this paper is based on the employment of syphilitic serum with alcoholic extract antigens of heart muscle. In this regard it is similar to the precipitation reactions of Meinicke, Sachs and Georgi, and Dreyer and Ward. . . . The test proposed, however, differs from each of these reactions in essential phases.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Induced Abortion, Followed By Fatal Hemorrhage and Sepsis

A thirty-nine-year-old primipara arrived in the hospital flowing profusely and evidently septic. She stated that her last period had occurred approximately four months before admission, and that an abortion had been induced. The previous medical history was irrelevant.

The patient's temperature was elevated, but the record does not state how high it was. Physical examination was negative except for an abdominal tumor mass, which rose above the symphysis and was consistent with the size of a four months' pregnancy. One foot was protruding from the introitus. Under aseptic precautions, the fetus was extracted and the uterus curetted of retained placenta tissue. The record suggests that a large part of the placenta was lying over the internal os, and when this was removed, a tremendous amount of blood followed. The patient went into extreme shock, and was given ergot, pituitrin and stimulants. The vagina and uterus were tightly packed with gauze, and the patient was returned to bed. She died shortly thereafter.

Comment. It is well recognized that artificial emptying of the uterus during the second trimester is very difficult, and that hemorrhage and sepsis frequently follow an attempt to induce such evacuation. This case is said to have been self-induced; at any rate, both sepsis and hemorrhage followed. No transfusion was given, and it is doubtful whether it would have been of any value, because the hemorrhage from a uterus at this period of gestation may be perfectly tremendous. There is little in the history to criticize. It is said

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, *Secretary*, 330 Dartmouth Street, Boston.

that the operation lasted twenty minutes. If the bleeding had continued from the first at a startling rate, it would have been more conservative to pack the uterus and permit some of the placenta to remain, rather than to continue the operation with the idea that the uterus must be emptied. This is the cardinal treatment of any criminal abortion. In the face of very active hemorrhage, all attempts to remove the products of conception should be postponed, the immediate hemorrhage should be treated by uterine packing, and the patient should be transfused while still alive.

DEATHS

BARNES — J. ARTHUR BARNES, M.D., of Worcester, died September 6. He was in his seventieth year.

A native of Fitchburg, Dr. Barnes received his degree from Harvard Medical School in 1900. He was a fellow of the American College of Surgeons, the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, a son, a brother and a sister.

STONE — FRANK E. STONE, M.D., of Lynn, died September 3. He was in his eightieth year.

Born in Lynn, Dr. Stone received his degree from Bowdoin Medical School in 1885. He was a member of the Massachusetts Medical Society and the American Medical Association. He was on the staffs of the Lynn and Union hospitals.

His widow, a son, two daughters and a sister survive him.

MISCELLANY

TUBERCULIN TESTING IN CHICAGO SCHOOLS

Findings in an extensive tuberculosis survey in Chicago schools, using the tuberculin test as a screen, are now available (*City of Chicago Municipal Tuberculosis Sanitarium Bulletin*, **18** [1938], **19** [1939] and **20** [1940]). Although it is not a new conclusion that routine skin testing in elementary-school groups is not an economical procedure, the report does contribute materially to knowledge of the epidemiology of tuberculosis and permits comparison with previous surveys in Chicago. An abstract follows:

This survey was carried out by the Chicago Municipal Sanitarium, aided by the Tuberculosis Institute of Chicago and Cook County.

The survey policy of the Municipal Tuberculosis Sanitarium had hitherto been largely oriented toward older groups. Tuberculin testing in the schools, therefore, represented a deviation from established policy and was undertaken to explore educational values, morbidity rates, and case-finding potentialities of a follow-up of the reactors and to check on existent case-finding machinery.

Since the purpose was to obtain a cross-section of tuberculosis morbidity, the survey attempted to include every Chicago school. However, it was necessary to sacrifice certain ambitions, such as a 100 per cent consent and a thorough survey of each school. In a general way, the policy ran, "Get what consents you can in the time allotted and go on to the next school."

Kindergarten children, those in the first and eighth grades and all available students in the high schools, were examined. It was thought that a positive reaction in a kindergarten or first-grade child might have some epidemiologic significance. Eighth-grade children, on the threshold of adolescence, were included because many would not go to high school; thus it might have been the last chance to include them in a case-finding effort. In view of the many studies already made, the justifiability of high-school examination is hardly debatable.

First, the Board of Education notified the principals. Then the nurse addressed the teachers and children in each room. All were given appropriate literature, which, with the consent card, the children took home. After a proper interval, a team did the tuberculin test, and the results were read in forty-eight hours.

In all, 176,878 consents were obtained in 561 public elementary schools, 115 public high schools, 347 parochial elementary schools, 47 parochial high schools, 12 trade and vocational schools and 5 junior colleges.

A self-contained and complete mobile unit, the first known to be used in the x-ray field, was devised. On starting work the truck drove into the schoolyard and the technician selected a location as near as possible to space for extra dressing rooms. Current was obtained through a cable from a school connection.

The procedure, carefully standardized, was to give a single Mantoux test, using PPD (purified protein derivative) in an amount one tenth the usual final dose. The percentage of reactors with this dose was low compared with the experience in other urban areas, so that the dose was doubled in the latter part of the work, except with Negroes and Mexicans, who had shown marked sensitivity to tuberculin.

In the 167,345 children tested, 27,401 proved positive. To March 1, 1940, 23,532 had been x-rayed and 218 cases of reinfection-type tuberculosis had been found, of which 109, or 50 per cent, were in the moderately or far-advanced stage; in 4524 children, evidence of primary-infection-type tuberculosis was found.

The reactor rate and the primary tuberculosis rate were practically the same for boys and girls, but the incidence of reinfection-type tuberculosis was twice as high in girls. The incidence of disease among children x-rayed was higher in Negroes and Mexicans but not to the same degree as the infection rate. The Negroes had slightly less primary tuberculosis than the Whites.

The study seemed to bear out the reports of other workers who found a lack of constant correlation between tuberculin sensitivity and tuberculous calcifications.

In comparison with other metropolitan surveys, the reaction incidence in Chicago is low. This may be because no person with an open case may live in the same home with children under sixteen: contact is broken as soon as possible after discovery of the case.

Survey results confined to a district or a constellation of districts would lead to false conclusions. The survey included schools in every district and children from every economic level. The major part of the tuberculosis problem is sharply localized. About four of the seventy-five census districts account for 38 per cent of the deaths. Mortality in these areas is much higher than the general rate, namely, 196 per 100,000, as compared with 51.6 per 100,000 for the city as a whole; morbidity figures also run in the same ratio.

In Chicago, as elsewhere, decreasing mortality rates probably exerted an influence on the composition of the infection index. The rate has fallen from 147.9 per 100,000 in 1917 to 51.6 in 1939. Over the same period, the rate has fallen from 133.9 to 34.0 for Whites and from 414.0 to 281.7 for Negroes.

In an attempt to estimate the diminution of the reactor rate, the present figures may be compared to older studies, one made by Webb of the University of Chicago in 1930–31, and the other by Novak and Kruglick of the Tuberculosis Institute of Chicago and Cook County in 1933–37. Webb tested no high-school children, and Novak and Kruglick tested no elementary-school children. In elementary-school ages, comparing Webb's figures with the present study, since 1930–31 there has been a definite drop for each age period. Comparing high-school tests for 1933–37 and 1936–39, there has also been a substantial drop for each age period, except for age twenty; only 29 students of this age were tested in the Novak study.

The specific relation between tuberculin-positive reactors and tuberculosis in the home was clearly demonstrated in the present survey. The source of infection was unmistakably established in 3284 cases, but of these only 226 were new pulmonary cases.

The comparatively small number of new cases found in the families of the positive reactors was both a disappointment and a satisfaction. A larger proportion of new tuberculosis had been anticipated, but it was encouraging to know that the existent case-finding machinery is effective, since in 90 per cent of the cases the source of infection was already under supervision.

Altogether, 586 new cases of tuberculosis were found. The total cost chargeable to the survey for the 586 cases found was $511.95 per case.

To explore its potentialities, figuratively speaking, the miniature x-ray machine was carried almost to the doorstep of the people in the congested areas. The equipment was hooked up to the mobile x-ray truck, and this self-contained unit, including dressing rooms, was taken to various locations.

The plan, still operative, aims at making an x-ray examination of every man, woman and child in certain areas of gross congestion, high tuberculosis mortality and low economic status.

In the school survey, lasting three years and comprising 23,532 x-ray examinations, 218 new cases were found on the first film. In the miniature x-ray survey, comprising 20,956 examinations and lasting five months, 675 new cases were found by the original x-ray film.

To summarize, during a three-year period, 167,345 children were tuberculin tested, and 23,532 x-rayed. The reactor incidence was 7.04 per cent for kindergarten and first grade, 19.82 per cent for eighth grade, 21.29 per cent for high-school students and 29.97 per cent for miscellaneous schools and colleges. The rate for Negroes was twice that of Whites, and for Mexicans it was still higher.

The study showed a substantial drop in the reactor rate in Chicago as compared with older studies. The city-wide survey emphasized the fact that each district had its own reactor rate, which was allied to local mortality rates.

In 57,481 children under twelve tested with tuberculin, 9 cases of pulmonary disease were found, which is comparable with figures for this age group in the mortality tables. Facts point toward the adolescent and early adult years as the case-finding provinces. In testing adults in highly infected milieus (60 per cent reactions or more), x-ray study of the entire group is cheaper than tuberculin testing, with x-ray examination of the positive reactors.—Reprinted, in part, from *Tuberculosis Abstracts*, August, 1941.

HARVARD MEDICAL SCHOOL

Award of sixty-five Harvard Medical School scholarships totaling $21,295, for study during the 1941–42 academic year, has been announced by Harvard University. The recipients of the scholarships are:

Chiu-an Wang, 1M, Hong Kong, China; Harold S. Robinson, 3M, Shantung, China; Robin G. Anderson, 2M, Passaic, New Jersey; Harold Brown, 2M, Dorchester, Massachusetts; Theodore G. Erler, Jr., 3M, Bellevue, Ohio; William J. Lahey, 3M, East Hartford, Connecticut; Sidney W. Ellery, 2M, Miami, Arizona; Elliot L. Sagall, 2M, Revere, Massachusetts; Grant V. Rodkey, 2M, Coeur d'Alene, Idaho; William Ridder, 1M, Bellingham, Washington; Thomas D. Allison, 2M, Kittanning, Pennsylvania; Robert L. Berg, 1M, Spokane, Washington; Logan O. Jones, 2M, Birmingham, Michigan.

James M. Judd, 1M, Randolph Center, Vermont; Frank E. Trobaugh, Jr., 1M, West Frankfort, Illinois; Duane H. Mitchel, 2M, Winchester, Kansas; John A. Evert, Jr., 3M, Glendive, Montana; Jesse E. Thompson, 2M, San Benito, Texas; Alvin T. Held, 4C, Columbus, Ohio; Paul A. Riemenschneider, Cleveland, Ohio; Bernard W. Robinson, Roxbury, Massachusetts; Boris P. Bushueff, 1M, Harbin, Manchu Ti-kuo; William R. Waddell, 1M, Tucson, Arizona; James E. Kreisle, 3M, Austin, Texas; Lindley B. Reagan, 3M, Poughkeepsie, New York; David W. Williams, 2M, Washington, Connecticut.

Francis R. Lane, 1M, Somerville, Massachusetts; Richard J. Cundiff, 2M, Long Beach, California; John Q. U. Thompson, 3M, Jacksonville, Florida; Edwin W. Peterson, 1M, Denver, Colorado; David S. Speer, 2M, Bronxville, New York; James H. Straugh, 3M, Canton, Ohio; Herbert R. Morgan, 3M, Bell, California; Harold F. Searles, 1M, Hancock, New York; Israel H. Scheinberg, 1M, New York, New York; Stephen L. Madey, 1M, Buffalo, New York; Harry D. L. Kaye, 3M, New York, New York; Daniel Sciarra, 1M, Paterson, New Jersey; Burdick G. Clarke, 3M, Winnetka, Illinois; James P. Dixon, Jr., 1M, North Rochester, New Hampshire; Charles Averill, 3M, Methuen, Massachusetts; Theodore S. Cobbey, Jr., 1M, Canton, Ohio.

Abraham N. Barger, 2M, Greenfield, Massachusetts; Melvin B. Black, 1M, Roxbury, Massachusetts; James T. Blodgett, 3M, Woburn, Massachusetts; Frederic B. Breed, 2M, Cambridge, Massachusetts; Donald E. Brown, 2M, Beverly, Massachusetts; Robert H. Brown, 1M, Hyde Park, Massachusetts; John Burbank, 2M, Lynn, Massachusetts; Allan D. Callow, 3M, West Somerville, Massachusetts; Dante F. Campagna-Pinto, 2M, Boston, Massachusetts; David Dove, 3M, South Sudbury, Massachusetts; Robert W. Gage, 3M, Needham, Massachusetts; Thomas V. Healey, 1M, Worcester, Massachusetts; Robert B. Higgins, Cambridge, Massachusetts.

Robert B. Holden, 2M, Stoneham, Massachusetts; Elmer V. Kenneally, 1M, Medford, Massachusetts; Eugene F. Poutasse, 1M, Weston, Massachusetts; Cornelius J. Shea, 2M, Dorchester, Massachusetts; Robert J. Tracy, 3M, Concord, Massachusetts; Paul F. Ware, 2M, Clinton, Massachusetts; Eugene L. Watkins, 1M, Worcester, Massachusetts; Albert E. Weiner, 3M, Newton, Massachusetts; Mark S. Wellington, 1M, Amherst, Massachusetts; and Frank C. Wheelock, Jr., 2M, Springfield, Massachusetts.

CORRESPONDENCE

SULFANILAMIDE SPRAY

In a letter published in the November 14, 1940, issue of the *Journal*, one of us (N. C. S.) suggested the use of a sulfanilamide spray in the treatment of colds and sore throats. Its local application in infected wounds has been used with considerable success, and it seemed reasonable to think that it would have a similar effect on inflamed throats and infected nasal passages.

Three 5-gr. tablets of sulfanilamide are dissolved in an ounce (30 cc.) of hot water. The tablets go into solution better if they are finely pulverized; however, even then, a sediment remains, which is liable to clog the atomizer. Sulfathiazole goes into solution better than sulfanilamide and appears to be equally effective, although our experience with it has been limited. When one is using sulfathiazole, two 7½-gr. tablets are dissolved in an ounce (30 cc.) of hot water.

We are convinced that the effects of the spray are markedly beneficial. The majority of colds and sore throats clear up in about half the time of the usual duration. It probably has no effect on the virus that causes the cold, but is markedly effective against the secondary invaders, and the earlier the cold is treated the better chance there is of holding the latter in check.

Colds that begin with inflamed throats give the most spectacular response. In a few hours, the redness fades, and the soreness disappears. A streptococcal sore throat rarely persists over twenty-four hours.

Since January, 1941, the beginning of the winter term, we have used the spray in the treatment of colds among the students of the Putney School. The days lost because of colds in the fall, winter and spring terms, compared with those of the two preceding years, are as follows:

1938–1939 (112 pupils).	Fall term	94 days
	Winter term	104 days
	Spring term	19 days
1939–1940 (122 pupils).	Fall term	180 days
	Winter term	128 days
	Spring term	39 days
1940–1941 (136 pupils).	Fall term	104 days
	Winter term	89 days
	Spring term	13 days

During 1940–1941, we had the best health record of any year since the founding of the school in 1934. Although we were in the midst of a severe epidemic of influenza, no serious illness occurred. There were only two cases of influenza, no cases of pneumonia, and no cases of bronchitis, which had been particularly bothersome in other years. There were a few cases of earache, but none that required paracentesis.

We do not mean to give the impression that the sulfanilamide spray was responsible for the small amount of illness, although we believe it was effective in stopping the invasion of tissues by secondary invaders, which in some cases ultimately result in sinusitis, bronchitis, pneumonia and otitis media. Furthermore, we believe it somewhat limits the contagiousness of colds.

At the Putney School, every child is inspected every day, and the slightest sign of a cold is treated immediately with the sulfanilamide spray. The treatment is continued every two or three hours for forty-eight hours, or until the cold has cleared up.

NEIL C. STEVENS, M.D.
MARIA PHANEUF, R.N.
Putney School
Putney, Vermont

REPORT OF MEETING

NEW ENGLAND PATHOLOGICAL SOCIETY

A regular meeting of the New England Pathological Society was held on May 17 at the Yale University School of Medicine, New Haven. Dr. Tracy B. Mallory presided.

The first paper, on "Wernicke's Hemorrhagic Polioencephalitis," was presented by Drs. J. P. Murphy, C. O. Prickett, A. J. Waring, Jr., and H. M. Zimmerman. Employing an experimental dietary regime in which thiamin and nicotinic acid were withheld or were given in small quantities, the authors reinvestigated the problem of the etiology of Wernicke's disease, with the rat as the experimental subject. All the other vitamins were given in amounts known or estimated to be adequate for this animal. Four groups of animals were used, and in the brains of those which received no vitamin B_1, or minimal amounts of it, the typical hemorrhagic and angionecrotic vascular lesions were found in the gray matter around the third and fourth ventricles and aqueduct of Sylvius. The nuclei of the vestibular nerves and of the cerebellum particularly were frequently and severely involved. The pathological findings were just as extensive when nicotinic acid was fed to the hypothiaminotic animals as when it was absent from the diet. From these studies, the investigators concluded that uncomplicated thiamin deficiency in the rat results in the production of lesions typical of Wernicke's disease; that concomitant deficiency in nicotinic acid does not significantly increase the number and extent of the lesions; that deficiency in nicotinic acid alone does not result in these changes; and that the longer the length of life of the animals not receiving B_1 the severer and more extensive the polioencephalitic changes tend to become. In the discussion, Dr. M. C. Winternitz asked whether it is known how the thiamin hydrochloride deficiency produces these changes. Dr. Zimmerman answered that thiamin hydrochloride has something to do with the metabolism of carbohydrate, and it is quite possible that its effect is similar to that produced by the deprivation of glycogen and glucose. It may, of course, have something to do with oxygenation in the central nervous system, producing anoxemic effects. He also noted that lesions of this kind due to vitamin B_1 deficiency have been seen in four species — the pigeon, rat, dog and man. Similar lesions are seen in man in the absence of alcohol, and the symptoms of those patients afflicted with Wernicke's syndrome are ameliorated by adequate amounts of thiamin hydrochloride.

The second paper, "Factors in Resistance to Tuberculosis," was presented by Drs. Bruno Gerstl and Robert Tennant. From the variance in response to the tubercle phosphatide when injected into rabbits or mice (Sabin, Thomas), it was concluded that the mouse cells are able to break down rapidly the tubercle lipoid, and that those of the rabbit do it at a slower pace, if at all. This ability of the mouse cells may be one of the additional factors on which the natural high resistance of the mouse to tuberculosis is based. It could be demonstrated that phosphatases alone were not able to break down the tubercle phosphatide. The previous action of a second enzyme, a lipase in a general sense, was necessary. Lecithinase "A" obtained from snake venom was one of the particular lipases facilitating further splitting; it could not be ascertained, however, in the parenchymatous organs of the mouse. Another lipoid-splitting enzyme was obtained from the mouse liver and differentiated from other esterases by using quinine as an inhibitor. Its action, com-

bined with that of phosphatases, effected 80 to 90 per cent splitting of tubercle phosphatide or lecithin, whereas either enzyme alone accomplished little. Comparison of the reaction velocities of phosphatases of the three species, mouse, rabbit and guinea pig, showed marked differences. When the tubercle phosphatide was used as substrate, the mouse enzymes produced a rapidly progressing cleavage, the guinea-pig lung, none at all; the effect of the rabbit organs was in between. Experiments in progress suggest that this difference is due not only to variations in enzyme concentrations but also to the inhibition exerted by the tuberculostearic acid split off from the phosphatide. This inhibition varies with the species from which the enzymes are derived. The discussion was opened by Dr. Valy Menkin, who stated that, a number of years ago (1928, 1929), Lurie, of the Henry Phipps Institute, demonstrated that rabbits infected with tubercle bacilli displayed differential destructive capacity in various organs. The bacilli were rapidly disposed of by the spleen, liver and bone marrow while, on the other hand, these micro-organisms persisted in the lungs and kidneys. There has been no adequate explanation offered for this difference in local organ immunity. Dr. Menkin wondered whether the findings of Dr. Gerstl on the splitting and liberation of phosphorus compounds could not yield a clue to this fundamental problem. In other words, is it possible that these same organs would yield differences in chemical activity that could in turn be correlated with the number of recoverable bacilli in the respective organs? He considered this to be of definite interest, since the speaker's thesis was apparently designed to show that some of the factors of resistance in tuberculosis are to some extent associated with the ability of tissues to split phosphatide compounds. He was not certain whether or not the last chart shown suggested the possible existence of any such quantitative correlation in the organs studied. Dr. Gerstl replied that Corper, in 1931, also demonstrated that canine lungs, liver and spleen are able to destroy tubercle bacilli when incubated for several weeks. The charts shown indicated that there is a difference in the rate of splitting the tubercle phosphatide when organ extracts of the same species — and, still more, when organ extracts of the mouse, rabbit and guinea pig — are compared. This ultimately results in a quantitative difference. These investigations differ from those first mentioned by the employment of purified extracts and by the attempt to determine the enzymes responsible for the breakdown of the tubercle phosphatide.

The third paper, "Experimental Brain Tumors Produced with Benzpyrene," was presented by Drs. H. Arnold and H. M. Zimmerman. Attempts at producing cerebral neoplasms with benzpyrene have in the past yielded uniformly negative results. In most of these experiments, the carcinogen was administered in an oily vehicle such as lard, cholesterol and lanolin, and only granulomatous reactions were produced at the sites of benzpyrene implantation. In the present experiment, 51 mice of the C-3-H strain had pellets of the pure carcinogen implanted in the right cerebral hemisphere. Up to the three hundred and twenty-fourth day of the experiment, 27 of the animals died or were killed, and of these, 22 had intracranial neoplasms. Eleven were gliomas, 10 were sarcomas, and 1 was a mixed tumor of gliogenous and sarcomatous origin. Included among the gliomas were 3 glioblastomas multiforme, 1 oligodendroglioma, 1 astrocytoma, 3 ependymoblastomas, 1 medulloblastoma and 3 unclassifiable gliomas. Most of the tumors have been transplanted successfully in the subcutaneous tissues of other mice of the same strain. It has been found that the tumor transplants are of great value in the classification of the experimental neoplasms because typical morphologic features, absent in the original tumors, frequently appear in the second and third hosts. In the discussion, Dr. Zimmerman stated that it is interesting to speculate on the reasons why previous benzpyrene experiments to produce intracranial neoplasms were unsuccessful. Perhaps the wrong animal was used, or, more probably, the carcinogen was inserted in the wrong vehicle. It is quite possible that the granulomatous change that may have been produced was too great, and killed the animal before the tumor developed. It is also interesting to speculate on how the carcinogen acts. Is it merely a catalyst? Since gliomas practically never metastasize outside the brain, it was believed that there must be some antagonism to the growth of ectodermal gliomas on the part of mesodermal tissue. The fact that these tumors have been successfully transplanted in subcutaneous tissue proves that there is no local antagonism. Dr. Mallory mentioned that he had seen a malignant teratoma of the ovary containing glial tissue, with omental implants of the glial tissue, and asked whether any of the mixed tumors had appeared in the transplant as mixed tumors. Dr. Zimmerman answered that it is possible to get mixed tumors in the transplant. On the other hand, transplantation of the mixed tumors is one method of separating them. One of the transplants may yield a glioma, and the other a sarcoma, a process quite analogous to the isolation of bacteriologic colonies.

The next four papers dealt with kidney and cardiovascular disease. The general survey of the experimental approach was presented by Dr. M. C. Winternitz. The results of bilateral nephrectomy in the dog have been found to contrast sharply in various ways with those following ligation of both main renal arteries. This has been pointed out for the blood pressure, which does not usually rise and never attains significant proportions after ablation of both kidneys, but which, as a rule, does become elevated after ligation of both renal arteries. Other contrasts, thus far not emphasized, involve survival time, rate of rise of blood nonprotein nitrogen, quantitative change of electrolytes of the blood with associated effects on cardiac function and, finally, the ultimate contrasting morphologic processes manifested after the two procedures. Moreover, the bilaterally nephrectomized animals have proved valuable for determination of the acute functional and structural effects caused by the injection of whole extracts and also of fractions of extracts of kidney and other organs of homologous and heterologous species. The results of these experiments have encouraged the utilization of similar extracts with normal dogs, and chronic counterparts of the acute processes are now being obtained. Dogs survive bilateral nephrectomy as long as ten days; the average is seven, and very few die before the end of the fifth day. The blood pressure shows little change. Vomiting occurs almost invariably. At autopsy, no specific gross lesions are encountered. Occasional subendocardial, valvular and visceral hemorrhages, as well as focal necroses involving heart muscle and smooth muscle of artery wall, alimentary or genitourinary canal, are rare but important findings. Ligation of the main renal artery of both kidneys may result in a moderate but definite rise in the blood pressure, which tends to fall again on the last day of survival of the animal. The nonprotein nitrogen of the blood rises rapidly, and by the third postoperative day equals that of the sixth day after bilateral nephrectomy. Vomiting is a prominent feature of the short clinical course. The animals give evidence of serious illness rather suddenly during the latter part of the second postoperative day and then become progressively ill, with signs of central-nervous-system irritation, includ-

ing nystagmus and, rarely, convulsions. The short survival period contrasts sharply with that of the nephrectomized animal. Death has occurred after ligation of both renal arteries not later than the fourth postoperative day, whereas animals whose kidneys have been removed often live twice, rarely three times, as long. The gross postmortem examination shows hemorrhagic lesions of wide distribution similar to those described as following much longer periods of hypertension and azotemia after constriction of the renal arteries. Edema, hemorrhage and necrosis of muscle, including heart muscle, smooth muscle of blood-vessel walls, hollow viscera and diaphragmatic muscle, are the lesions encountered. It should be emphasized that a minimal representation of the extensive anatomic changes found after ligation of both main renal arteries may be demonstrated by detailed examination when death follows removal of the kidneys. Consequently, absorption from the necrotic kidneys cannot be considered the only responsible factor. After ligation of both ureters, the lesions encountered, except for those of the kidney, conform to those that result after ligation of both main renal arteries. The results of the injection of extracts of necrotic and of normal dog kidneys into the bilaterally nephrectomized dog are strikingly similar. The injection may be associated with a slow rise in blood pressure, which reaches a maximum only after several minutes and then falls very gradually over an even longer period before it drops to the preinjection level. Nystagmus, vomiting and occasional convulsions may occur, with or without fall in pressure. The blood nonprotein nitrogen of the injected animal has a tendency to rise abruptly, as that of the ligated animal does. This rise is not due to the nitrogen content of the injected protein. The anatomic changes duplicate those that follow ligation of both main renal arteries. Their extent is associated both with the survival time of the animal and with the amount of extract received. Crude extract of pig kidney, obtained by the Buchner press or the Latapie technics and injected into nephrectomized dogs, has the same effects as dog kidney extract. The depressor effect is more constant than with dog kidney preparations. Dialyzation does not deprive the extract of either its vasopressor or its dilator properties. Intravenous injection of tissue extracts, as is well known, exerts a profound effect on blood coagulation time and actual clot production. It should be emphasized that many of these effects are encountered after partial or complete renal arterial or ureteral occlusion and that they include both vasal depressor and pressor actions, changes in blood nonprotein nitrogen, and electrolytes, hemorrhage and necrosis of muscle, including both heart muscle and the smooth muscle of blood vessel walls, and hollow viscera particularly. These occur in various combinations, and the fact that at least some may be eliminated by particular treatments indicates their separate origin.

One aspect of this problem, "Electrolytes, Potassium in Particular, and Cardiovascular Renal Disease," was presented by Dr. S. H. Durlacher. The electrocardiographic findings in potassium poisoning are similar to those seen in experimental renal insufficiency produced in animals receiving a normal diet. The serum potassium reaches lethal levels following extirpation of the kidneys and bilateral ligation of the renal arteries or ureters. The survival time of rats fed a diet deficient in potassium with consequent diminution of muscle and serum potassium, is significantly increased following the above procedures over animals fed a control diet. The animals die after a prolonged period, with markedly elevated blood nonprotein nitrogen. The serum potassium levels are not within the fatal range at the time of death. Hypertrophy of the rat kidney, which occurs after a three-week period on a low potassium regime, consists in dilatation of the tubules of the medulla and pyramid, with hyperplasia of the lining epithelium.

Another aspect of the subject, "Tissue Extracts, Blood Coagulation and Associated Anatomical Changes," was presented by Dr. R. Katzenstein. The well-known effects of tissue extracts on the clotting time of the blood and the production of thrombi are related to their content of thromboplastic substance. This varies considerably with different tissues. Lesions of the wall of heart and blood vessels are not necessary for thrombosis. Moreover, such mural changes occur without superimposed thrombi if the stability of the blood from the standpoint of its coagulation is not advantageous. Location of thrombi after injection of tissue extracts indicates variation in the coagulation time of the blood in different parts of the vascular bed and suggests that different organs participate in effecting the balance of the coagulation time.

Finally, the "Contributions to Cardiovascular Renal Disease from the Biochemical Approach" was presented by Dr. E. Mylon. Renin, the pressor substance present in normal renal tissue, was shown either to be attached to or to be a small molecular protein that is not precipitated by centrifugation at speeds of 50,000 revolutions per minute. Purification of the material diminishes the angionecrotic activity, although a blood pressure rise of 30 mm. of mercury is produced when quantities equivalent to 1 gamma of nitrogen per kilo are administered. This pure product is free of all enzymatic action, in contrast to the less-refined "renin-C" of Page and his co-workers. The necessity of an intermediary product such as "angiotonin," produced by Page, is questioned in the light of previous experiments by Landis, Montgomery and Speekman, who showed that the pressor substance acted only in the presence of an intact sympathetic nervous system. The failure of renin to produce contraction of an isolated artery is therefore not surprising. The depressor activity of crude kidney extracts, as well as similar preparations of other organs, is related to the thromboplastic activity of these products. When clot formation is inhibited by heparinization or by the postinjection negative phase of blood clotting, only a slight fall in blood pressure occurs. Kidney extracts do not, therefore, possess a strong depressor substance, and the sharp and sustained fall in pressure observed following the injection of these materials is dependent on their thromboplastic action. In the discussion, Dr. Menkin referred to his observations made recently on some preliminary studies on the subject of shock. This was induced by utilizing the method described by Dr. Walter B. Cannon a number of years ago, which, in brief, consists in studying blood-pressure changes after severe injury induced in the thighs of cats by crushing the muscles. The blood pressure is measured by the usual technic of introducing into the carotid vessel a cannula connected to a mercury manometer. In his experience, almost immediately after the severe injury has been induced, there is a sharp drop in blood pressure, which is sustained throughout the period of the acute experiment. This may last one or two hours. Furthermore, it is of interest that in these animals the rate of blood coagulation seems to be hastened, as evidenced by the frequent necessity of washing clots from the carotid cannula, a state of affairs not observed in animals with uninjured tissues. In view of the very interesting observations of extracts of tissues favoring the formation of thrombi, Dr. Menkin wondered whether thromboplastic substances may not be constantly diffusing into the circulation from an area of extremely

(Continued on page xii)

Windmill in 18th Century Shropshire

The Birthplace of Digitalis

Dr. Withering practised medicine in Shropshire, England, and it was there that he made his epochal studies on the foxglove. The plant had been known for centuries, but as a heart tonic, clinically evaluated, the work of Withering made it available to the medical profession in 1785. A century and a half have elapsed since then. During most of those intervening years physicians and pharmacists have been harassed by the vexing problem of producing digitalis in more stable forms. The painstaking work of the research laboratories of Hoffmann-La Roche led to the development of Digalen 'Roche'. From the clinical standpoint this work has received gratifying acceptance. Many critical clinicians consider Digalen their digitalis of choice. One reason for this preference is the rigid adherence to standard potencies, expressed in cat units. Every effort is made to prevent any deviation, either below standard or above standard.

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(Continued from page 432)

severe tissue injury. In answer to the question what the brain showed in the animals whose kidney vessels were ligated, Dr. Zimmerman said that in those animals in which the renal arteries were ligated, the brain was normal. In those in which the ureters were ligated, the brain showed angionecrosis, hemorrhage and softening, and in some, even dissecting aneurysms of the smaller cerebral arteries. The lesions were similar to those seen in Wernicke's disease, except for their distribution. In these experiments, the lesions were diffuse. Dr. Winternitz stated that occasional small pulmonary infarcts were noted, and that these were not at all embolic but were the result of local thrombosis.

NOTICES

ANNOUNCEMENT

Dr. Julius Loman announces the removal of his office from 1284 Beacon Street, Brookline, to 520 Beacon Street, Boston.

MASSACHUSETTS SOCIETY OF X-RAY TECHNICIANS, INC.

The list of speakers and their subjects that have been scheduled for the 1941–1942 meetings of the Massachusetts Society of X-Ray Technicians, Inc., is as follows: September 23, at the Massachusetts Memorial Hospitals, "Roentgenologic Study of the Gall Bladder," Dr. George Levene, and "Chemistry and Functions of Gall-Bladder Dyes," Dr. R. C. Page; October 28, at the New England Baptist Hospital, "Simplified X-Ray Technic," Dr. Magnus Smedal, and "Effect of Voltage on Radiographic Contrast and Density," Mr. Fred Schoeck; November 25, at the Massachusetts General Hospital, "Roentgenologic Examination of the Chest," Dr. Aubrey O. Hampton, and "Film," Mr. George Struck; January 27, at the Boston City Hospital, "Use of Opaque Materials in X-Ray Examinations," Dr. Paul F. Butler, and motion-picture film, "Moving X-Rays"; February 24, at the Palmer Memorial Hospital, "Practical Suggestions for the Therapy Technician," Dr. Joseph Marks, and motion-picture film, "Exploring with X-Rays"; March 24, at the Faulkner Hospital, "Fractures and Pseudo Fractures," Dr. Harvey Morrison, and "A Special Appliance for Shoulder Technic," Mr. Nathaniel Vadala; April 28, at the Lynn Hospital, "Roentgenologic Examination of the Abdomen," Dr. Herman A. Osgood, and "Protective Measures in Radiographic and Dark Rooms," Mr. Edward Parker; May 26, at the Beth Israel Hospital, "X-Rays in Urology and Gynecology," Dr. Samuel A. Robins, and motion-picture film, "Intravenous and Retrograde Pyelograms."

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, September 14

Wednesday, September 17

*12 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

September 16–18. Clinical Congress of the Connecticut State Medical Society. Page x, issue of July 17.

September 23–May 26. Massachusetts Society of X-Ray Technicians, Inc. Notice above.

October 8–10. American Academy of Pediatrics, Boston.

October 13–24. 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

October 14–17. American Public Health Association. Page 579, issue of March 27.

October 19–23. American Academy of Ophthalmology and Otolaryngology. Page 359, issue of August 28.

October 29–30. New England Postgraduate Assembly. Pages ii–iii.